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PRIMARY RETROPERITONEAL TUMOURS

By HANS HENRIK HOLM

In current textbooks, primary retroperitoneal tumours are treated rather summarily; either they are not mentioned at all or at the most they are dealt with in a few lines in small print. The literature on the subject in Denmark is, similarly, scanty. This fact, together with the fact that retroperitoneal tumours, despite their relative rarity, are of importance not only to the general surgeon but also to the urologist and gynaecologist have caused the author to take the subject up.

Further, a report is available from this department on the primary retroperitoneal tumours operated on during the period 1914—34 (37), and it was therefore considered of interest to follow this account up by publication of the nine cases treated for the same condition in the department during the years 1935—59. These cases are supplemented by two cases submitted to operation in Department I of the hospital.

HISTORY

Lobstein was the first to define the term retroperitoneal tumour in 1829 but the earliest available descriptions of such tumours originate from Morgani in 1761. The most extensive Danish work on the subject was published by Fleischer-Hansen in 1935 (7).

DEFINITION

Since the term "retroperitoneal tumour" was first proposed by Lobstein, delimitation of this type of tumour has been vague.

Lobstein included in this term both primary and secondary tumours. (Secondary tumours originate as a rule from tumours of the gonads). Since then, the limit for this group of tumours was established more exactly: metastases and, similarly, neoplasms originating from the retroperitoneal organs were excluded. Lymphosarcomata, reticulosarcomata and Hodgkin's disease are included in the group by many authors (1, 32, 39). It is well known that all varieties

from the localized (*e.g.* retroperitoneal) lymphosarcoma and reticulosarcoma to lymphatic leukaemia and monocytic leukaemia may occur. While isolated retroperitoneal lymphosarcoma and reticulosarcoma must be covered by the definition, it does not appear reasonable to include retroperitoneal tumours which have developed as part of a definite systemic disease (*e.g.* Hodgkin's disease and lymphatic leucosis). If this were the case the relatively uniform clinical picture presented by genuine retroperitoneal tumours would, despite their differing natures, be considerably obliterated.

As a conclusion from these deliberations, in the present article genuine primary retroperitoneal tumours will be considered to be tumours which have developed in the retroperitoneal space when tumours of the viscera, metastases and tumours which are part of systemic disease are excluded.

The Retroperitoneal Space

No natural limit of the retroperitoneal space exists but the limits suggested by Newmann & Pinck (32) appear reasonable: Superiorly, the 12th thoracic vertebra and 12th rib, laterally, the lateral margin of the quadratus lumborum muscle and inferiorly, the base of the sacrum and the iliac crest.

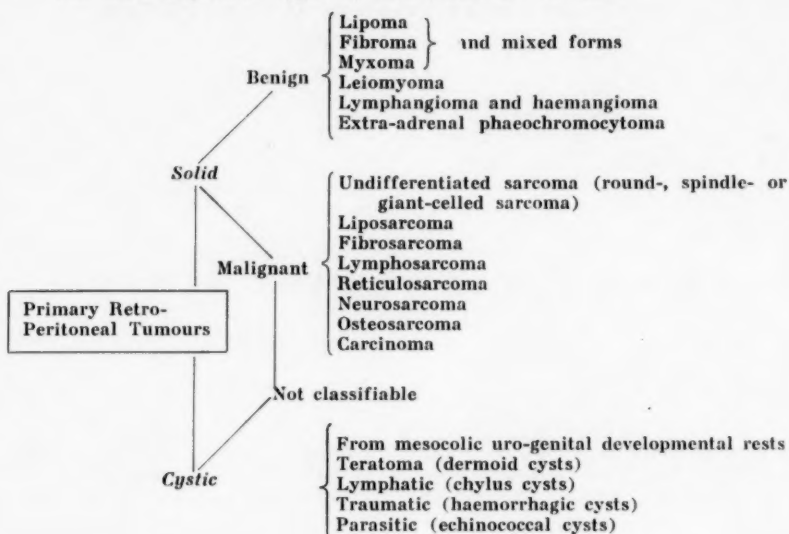
This space, the anterior and posterior limits of which are the parietal peritoneum and the posterior wall of the abdominal cavity, is filled with loose connective tissue traversed by numerous important structures: aorta, inferior vena cava, vessels to the kidneys and gonads, ureters, sympathetic ganglionic trunk, numerous nerves and, further, a chain of lymph glands.

ETIOLOGY AND HISTOGENESIS

As a rule it is stated (1, 9, 22) that the solid retroperitoneal tumours originate from the retroperitoneal loose connective tissue, adipose tissue, fasciae, lymph glands, vertebrae or nerve structures, but isolated authors (7, 14), among whom

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Table 1.
The More Important Types of Retroperitoneal Tumours.



are Hansmann & Budd, consider that both solid and cystic tumours may have a common etiology and develop from rests of the embryonic urogenital apparatus.

While considerable uncertainty reigns as regards the origin of the solid retroperitoneal tumours, plausible explanations appear to be available concerning all the *cystic* neoplasms.

An explanation of the rise of the *urogenital cysts* may be found in the complicated embryological development of the urogenital apparatus. This will not be discussed in detail but it will merely be recapitulated here that there are three renal precursors: Promeso- and metanephros which more or less disappear and, in addition, two tract systems: Wolffian duct and Müller's duct in addition to the precursor of the gonads. Should co-ordination of this complicated tract system fail at one point or another, the possibility of cyst formation arises.

The development of *mesocolic cysts* was described by Handfield-Jones (13): The ascending and descending colon in the beginning of embryonic life are situated intra-peritoneally with mesenteries and at a certain stage they swing back towards the parietal peritoneum so that three layers of peritoneum come to lie over one another. The two posterior layers which are placed mesothelium against mesothelium disappear but small islets may persist and possibly become the point of origin of a retroperitoneal cyst. According to the nature of the condition, such cysts come to lie between the ascending colon and the descending colon and under the transverse colon.

Many different theories exist regarding the mode of origin of *teratomata* and *dermoid cysts*.

Handfield-Jones adheres to the postulate made by Felix that they arise from retained but early developed totipotent sex cells.

Cyst formation in the retroperitoneal *lymphatic* system has probably an obstructive or rather a development cause (38). Should this occur in a lymph vessel coming from the intestine, formation of a chylus cyst containing milky fluid results.

Haemorrhagic cysts and *echinococcal cysts* which are so rare in this country do not merit any special mention.

HISTOLOGY

Not only here but also in the following section, this article will limit itself to a condensed review of the more important types of tumour.

Lipomata occur in the pure form and as mixed tumours. According to von Wahlendorf (46), who collected a material of 165 lipomata from the literature, 46 per cent were pure lipomata while the remainder consisted of 20 per cent fibrolipomata, 10 per cent myxolipomata, 10 per cent fibromyxolipomata and, further, 14 per cent in which sarcomatous degeneration had occurred.

Pemberton & Witlock (35) in a group of 30 cases found malignant degeneration in 10 per cent at the first operation. When cases are included in which microscopic examination at re-operation on account of recurrence showed sarcomatous degeneration, the percentage rose to 33. Lind (27) also stressed that certain reservations must be taken when dealing with these lipomata. He stated that even if meticulous, microscopic examination did not reveal malignancy, sarcomatous parts may, nevertheless, be found fre-

quently after one or more recurrences. Schmidt (40) goes even further and considers that half of these tumours described as benign are, in fact, malignant.

According to Golden & Stout (11), retroperitoneal *leiomyomata* in which the presence of myofibrils are necessary to establish the diagnosis have a great tendency to malignant degeneration but the *leiomyosarcomata* which develop in this manner are frequently of low grade malignancy.

Lymphosarcomata consisting of uniform round hyperchromatic cells dominate the markedly malignant tumours and are followed by the undifferentiated *spindle cell sarcoma* and *fibrosarcoma* (1, 32).

The tumour originating from striped muscle, viz the very malignant *rhabdomyosarcoma*, which according to Boyd is extremely rare and only exceptionally mentioned by the other authors, assumes a dominating position in Pack & Tabah's material as 22 out of 120 retroperitoneal tumours were said to be *rhabdomyosarcomata* (34).

Liposarcomata, the microscopic picture of which varies greatly, in the different cases according to Boyd (4), are easily overlooked.

Cysts frequently consist of a fibrous wall lined with flat epithelium. "Wolffian cysts" are limited by low cubical to high cylindrical epithelium and there may be primitive glomeruli and tubuli in the walls (24).

Teratomata are tumours composed of components derived from more than one embryonic layer. They may contain hair, sebaceous glands, teeth etc., and may occasionally undergo malignant degeneration.

Quite a considerable numerical group of retroperitoneal tumours must be placed in the category of *unclassifiable tumours* on account of absence of characteristic findings and mixed cell types.

MACROSCOPIC EXAMINATION

One feature that all types of solid retroperitoneal tumour have in common is that they may attain considerable size. While retroperitoneal sarcomata seldom attain a size greater than a human head (44), monstrous forms may be found among the slowly growing tumours, e.g. 31.4 kg (Hirsch & Well's 1920) (18). Pemberton & Witlock found the average weight of 5.6 kg in their material of 30 cases of retroperitoneal tumour which came to operation.

The solid tumours are, as a rule, coarsely lobulated. The majority are encapsulated. Lipomata are soft, show pseudofluctuation and are yellow in section. When the fibrous tissue content is greater, the tumours are more solid and whiter.

At the commencement, sarcomata are white or pink and hard and massive, and have a distinct tendency to degenerative changes resulting in necrosis, calcification or central cyst formation.

Steele (44) states that 35 per cent of sarcomata are cystic.

In its most typical form, lymphosarcoma appears as a fused mass of enlarged lymph glands which are greyish and homogeneous in section.

It has been stressed from various sources (7, 9) that even the malignant retroperitoneal tumours rarely show any invasive tendency of significance but this postulate is not in agreement with the findings of the majority of other authors nor does it correspond with the findings in the present material.

The commonest cysts (urogenital, mesocolic) lie freely in the retroperitoneal space, are thin-walled, unilocular, without adhesions and with thin liquid contents. Occasionally they may become very large.

LOCALIZATION

The most common site of origin of retroperitoneal tumours is lateral to the vertebral column and more rarely they are median. Tumours originating to the left of the vertebral column appear to preponderate (14, 35).

Very large tumours (lipomata and mixed tumours) in addition to being responsible for considerable displacement of the abdominal organs, may grow down over the sacrum into the true pelvis (9) or project forwards under the inguinal ligament and appear as a swelling distal to this (22). Further, such tumours may grow in through the vertebral foramina and produce medullary compression (4) and, finally, they may invade the mesentery and the mesocolon, and according to Keen (22) the lipomata found in these situations have practically always developed in this manner.

AGE DISTRIBUTION

While cysts occur electively in the younger age groups and lipomata in middle aged patients (22, 32) the distribution of retroperitoneal sarcomata, according to Steele, is such that this tumour form is quite common in the age group 0—5 years (10), very rare in the 10—20 age groups and thereafter the incidence increases until the age of 60 years. The oldest and youngest patients in Steele's material were 78 years old and under one year, respectively.

SEX DISTRIBUTION

Regarding retroperitoneal tumours as a total group, Donnelly (5) and Judd & Larson found a preponderance of these tumours in males in their materials (1.5:1 and 2:1). Various authors (7, 32, 34, 35, 46) found lipomata to be more frequent in females; Wahlgren found a sex distribution of 72 per cent females to 28 per cent males. Cysts are also stated to be most common in females (7, 14), while sarcomata, according to Steele, are most common in males (in his material 35 males; 23 females).

INCIDENCE

According to Scanlan (39) approximately 900 cases of retroperitoneal tumours have been described in the international literature. Pack & Tabah (34) state that 0.2 per cent of all tumours which were treated over a long period of years in The Memorial Cancer Center were situated retroperitoneally. In this department during the period 1914-34, six cases of these tumours were encountered among 42,000 admissions (37). During the period 1935-59 (covered by this investigation) nine cases were diagnosed from among 67,000 admissions.

SYMPTOMS

As long as retroperitoneal tumours are quite small, they do not give rise to any symptoms but as their size increases, vague symptoms appear such as slight dyspepsia, nausea, sensation of distension, loss of appetite, constipation or diarrhoea and occasionally dysphagia (22). Simultaneously, abdominal or lumbar pain most frequently of an aching nature may occur but this may also be of a boring or colicky nature. Frequently the pain is relieved by lying in the prone position (25). Occasionally, but not often, slight neuralgiform pains in the lower limbs are described.

When malignant tumours are present, considerable loss of weight, anaemia and occasionally pyrexia often occur.

Not unusually, the first the patient notices is the increasing abdominal circumference or a subjective sensation of "a swelling in the belly". In Pack & Tabah's material of 120 patients, this occurred in 30.8 per cent of the cases.

Urological complaints are strikingly rare even although the kidney may be very markedly dislocated or completely surrounded by the tumour (7). Patients complain occasionally of pollakiuria and in very rare cases, the tumour may cause uraemia on account of bilateral constriction of the ureters (37). According to Newman & Pink, a retroperitoneal tumour may influence the functions of the bladder and the rectum and thus simulate prostatic disease.

The common bile duct may be greatly displaced and course over the tumour but jaundice practically never occurs (7). On the other hand a case of Budd-Chiari's syndrome (obstruction of the hepatic vein with hepatic stasis, ascites and abdominal pain) produced by an expanding retroperitoneal sarcoma has been described (26).

Acute episodes such as intestinal obstruction or perforation thus only exceptionally occur in retroperitoneal tumours. In his material of 75 cases, Fleischer-Hansen did not find any such episodes. This forms a sharp contrast to the mesenteric tumours in which an "acute abdomen" frequently develops very early.

The average duration of symptoms for patients with retroperitoneal tumours was 4.2 months in

Pack & Tabah's material. Fleischer-Hansen, however, had experience which deviated considerably from this and he states that these patients on the whole seek medical advice very late. In his material, lipomata had thus produced symptoms for three years and sarcomata for 14 months before the patients sought treatment.

When the patient eventually seeks medical advice, a distinctly palpable abdominal tumour is nearly always felt, although at the commencement this is felt far back in the abdomen. In the majority of cases, the tumour cannot be moved, or, in any case, is only slightly moveable manually and with respiration. The tumour is frequently situated to one side of the midline and is frequently lobulated and may show pseudofluctuation (lipoma) or may be hard (sarcoma, fibroma).

The tumour may dissect between the two layers of the mesocolon and, finally, the ascending colon, descending colon and, in higher medial tumours, the transverse colon come to lie in a groove on the anterior surface of the tumour. This gives the possibility for a very characteristic finding on percussion: A tympanic band is found across the tumour and the small intestine is displaced to the opposite side (44).

The increasing growth in the abdomen may cause venous stasis with oedema of the lower limbs, increased abdominal venous marking or rapidly increasing hydrocele which may be mistaken for a primary tumour (6).

An interesting symptom of retroperitoneal tumour is that described by Hess in 1929: A space-occupying retroperitoneal tumour may, at the commencement (on account of irritation of the lumbar sympathetic trunk on the same side) cause reduction of the temperature of the corresponding lower limb. Later, paralysis of the nerves may result in increased temperature. The difference in temperature may be 2-3° C and can frequently be appreciated by the hand and can otherwise be detected by means of an ordinary thermometer. Further, there are simultaneous changes in the secretion of sweat. These symptoms are stated to appear very early and may possibly be the only symptoms (47).

The symptoms are aggravated as the tumour gradually increases in size. Ascites develops late and finally the patient may be thin and cachectic in great contrast to the very distended abdomen. Displacement of the diaphragm may embarrass the function of the heart and lungs.

Finally, it should be mentioned that, in rare cases, the singular phenomenon may be encountered that a retroperitoneal tumour (or more rarely, an intrathoracic tumour) may cause severe hypoglycaemia which may possibly prove fatal.

According to Howard & Davis (20) 15 cases of hypoglycaemia caused by swellings not originating in the pancreas have been described.

Of these, nine were cases of retroperitoneal tumour, mainly fibromata and fibrosarcomata (20, 41).

The mode of origin of the hypoglycaemia is uncertain. Hines (17) suggest the possibility that a product of the metabolism of the tumour may influence the pancreas so that the insulin activity is increased or, as another possibility, that the carbohydrate metabolism of the tumour cells is very great.

Skillern (43) described two case and Holten (19) one case which they regard as a typical islet-cell tumours which resembled spindle-cell sarcomata.

Scholz, Wooler & Priestly (41), on the other hand, consider that their own two cases and the other cases which have been described have been more or less undifferentiated fibrosarcomata. Seckel (42) mentions the possibility that the tumours (which are always large) by paralysis of the sympathetic innervation of the liver influence the blood sugar level. This is, however, considered improbable, one of the reasons being that also tumours situated above the diaphragm and in the left side of the abdomen may produce the same effect. According to Mirsky (30) the reason for the hypoglycaemia may be that the tumour secretes a substance which acts as an inhibitor of insulinase or competes with insulin for insulinase. Holten emphasizes that biological tests for hypoglycaemic factors and tests for the insulin content of the tumour should be undertaken in these rare cases in which hypoglycaemic attacks are a dominating feature in the symptomatology. This has been attempted without success in several cases (20, 41, 42), but recently, August & Hiat (3) in an intrathoracic fibrosarcoma weighing 1370 gm demonstrated insulin-like activity corresponding to 600 units of insulin.

DIAGNOSIS

The diagnosis of retroperitoneal tumour is difficult. In several materials correct pre-operative diagnosis was established in less than half of the cases (7, 32).

Out of the various clinical findings Steele states that the situation of the intestine on the anterior surface of the tumour is one of the most important signs. Steep & Bøger (45) state that retroperitoneal tumours do not fall further forwards in the abdomen when the patient assumes the knee-elbow position in contrast to benign retroperitoneal tumours and other abdominal tumours.

Ordinary laboratory investigations do not provide any particular information apart from the fall in haemoglobin level and the increase in the ESR found in cases of malignant tumours. Exceptionally rarely, occult intestinal haemorrhage may occur and only exceptionally haematuria

(on account of venous stasis in the kidneys or extension into the renal pelvis) (6, 7, 32).

Radiographic examination of both the urinary tract and the alimentary canal is of great significance for the correct diagnosis. Intravenous urography or direct pyelography with lateral exposures may frequently, on account of dislocation of the kidney or ureter provide convincing evidence of a retroperitoneal growth. Donnelly states that in the tumours in which radiologically demonstrable dislocation of the ureter is present, the diagnosis of retroperitoneal tumour is frequently certain as the ureters are adherent to the posterior parietal layer of the peritoneum and, therefore, anything which displaces them anteriorly or laterally must be retroperitoneal. A pyelogram in which both kidneys are shown on the same side of the midline is practically pathognomonic of retroperitoneal tumour (this occurs otherwise only in the very rare cases of crossed renal dystopias) (7, 48). Nephrotomography may also be of value in determination of the localization of the tumour in relation to the kidney.

Radiographic examination of the gastrointestinal tract should be undertaken both as straight X-ray photographs and following introduction of radio-opaque media (orally and rectally). In cases in which the tumour is situated posteriorly to the ascending colon or the descending colon on account of the anterior displacement of the intestine, direct evidence may be obtained that the tumour actually is retroperitoneal. In other cases, the information obtained by this investigation is less certain but it can, however, demonstrate that the tumour is extraintestinal.

The following more specialized diagnostic aids may be mentioned: retroperitoneal insufflation of air, aortography, abdominal venography and determination of adrenal line when (extra-adrenal) pheochromocytoma is suspected.

Finally, there are numerous cases in which the diagnosis is not established until exploratory laparotomy or explorative lumbar incision are performed.

DIFFERENTIAL DIAGNOSIS

The differential diagnostic possibilities are numerous.

Retroperitoneal tumour may be confused with any swelling of the kidney, e.g. hypernephroma, hydronephrosis, cystic kidney, or perinephric abscess. It may present in the lumbar region as do renal tumours and even produce "renal ballotement" (7). The urograms are frequently useful in this connection as the retroperitoneal tumours, as mentioned already, only cause greater or lesser dislocation while, as a rule, in true renal lesions characteristic deformation of the urograms is encountered.

Apart from the cases in which the symptomatology is characteristic on account of the disturb-

ances in hormone production (Cushing's syndrome, pheochromocytoma), suprarenal tumours may be impossible to distinguish from genuine retroperitoneal tumours without explorative laparotomy (21, 44).

Tumours in the gastro-intestinal canal, peri-appendicular abscesses, swellings of the liver and pancreas and splenomegaly may be very difficult to distinguish from retroperitoneal tumours (2, 5, 7, 21, 32, 44, 45).

Mesenteric and omental cysts are very mobile and their clinical picture is, as a rule, more acute but these may occasionally be confused with retroperitoneal cysts (7, 32).

Retroperitoneal tumours which extend into the true pelvis may be very difficult to distinguish from ovarian or uterine tumours in females (5, 21, 32, 40, 44).

Problems in differential diagnosis may also be caused by cystically degenerated tuberculous glands (7, 23, 44), dissecting aortic aneurysms (44, 45) and systemic diseases with predominantly abdominal manifestation (45).

According to Fleischer-Hansen cases of tumours of the gonads with retroperitoneal metastatic tumours as the dominating feature are very rare but this possibility should not be overlooked.

Finally, mention should be made of a condition which may simulate retroperitoneal tumour, not on account of the findings on palpation but on account of its obstructive tendencies. The rare condition termed "periureteritis fibrosa" or more correctly "idiopathic retroperitoneal fibrosis" is concerned. This occurs as a progressive fibrosis which spreads laterally in the retroperitoneal space and gradually surrounds, twists and, finally obstructs both ureters (more rarely only one is affected) finally producing anuria and uraemia. The etiology is unknown but a tumour pathogenesis can be excluded (8, 10, 12, 25, 28, 31).

TREATMENT

The treatment may be operative removal, radiation therapy or a combination of these two possibilities.

Cysts are, as a rule, not difficult to remove. The operative mortality is considerably lower than with the remaining retroperitoneal tumours. Fleischer-Hansen gives the mortality as 4 per cent and Frank as 8 per cent. No more extensive accounts are available but there can be no doubt that the percentage of recovery is also considerably better than in the solid tumours (7, 14, 22). Very large or adherent cysts which are difficult to remove operatively may, according to Lahey & Eckerson, be treated with good results by marsupialization after a period of drainage.

Nearly all authors state that the treatment of all the solid retroperitoneal tumours, both benign and malignant, must primarily consist of total

extirpation (or an attempt at this), if this is at all possible.

The *operability* of retroperitoneal tumours as a whole, probably on account of incomparable materials, appears to vary greatly according to the statements from various authors. Frank found that 89.9 per cent of his material was operable, Donnelly 35 per cent and Duval only 11.4 per cent (from materials of 99, 95 and 39 patients, respectively).

The *operative mortality* is also reported to vary greatly (5, 7, 9, 34, 35, 40). This depends, naturally, upon the type of tumour. Fleischer-Hansen thus reports a mortality of 32 per cent for malignant tumours and 12 per cent for benign tumours. Frank agrees with this and states that for relatively benign tumours such as fibromata and lipomata the operative mortality is 8 per cent, for myxomata 18.8 per cent, for sarcomata 28.3 per cent and, finally, for teratomata 36 per cent. Pack & Tabah found an operative mortality of 10.8 per cent among all their cases of retroperitoneal swellings submitted to operation.

While the results of surgical treatment in definitely benign retroperitoneal tumours are, on the whole, good they are much less satisfactory in lipomata and mixed tumours where, even after apparently complete extirpation of the tumour, recurrence may often take place (22, 27, 35). Thus Pemberton & Witlock, in their material of 30 patients with retroperitoneal lipomata, found satisfactory results of surgical treatment in only half of the patients. Six patients died in connection with the operation and nine out of the remaining 24 developed recurrences.

The results with sarcomata (derived from connective tissue and also those which develop from lymphatic tissue) are even poorer. In such cases it is rare that the diagnosis is established so early that complete extirpation of the tumour (essential for a favourable result) is possible. Among his 27 patients with primary retroperitoneal sarcomata (most frequently lymphosarcomata, and thereafter the undifferentiated sarcomata and fibrosarcomata), Andrews found only seven to be operable. Out of these one died on the day after operation and five shortly afterwards from recurrences.

The operative technique: The operative possibilities available are the lumbar approach (extraperitoneal) and laparotomy (transperitoneal). The latter intervention on account of the better access and the greater possibilities for radical operation is preferable and is employed in the vast majority of cases.

During operative intervention upon retroperitoneal tumours complications frequently occur, which necessitate e.g. splenectomy, intestinal resection or most frequently nephrectomy (a thorough investigation of the renal function and the urinary tract is, therefore, always essential preoperatively (5, 7, 22, 34)).

While general agreement exists that radiation in certain cases is of considerable value as a supplement to the surgical treatment (5, 6, 9, 32, 34) and in many cases is the only treatment which can be undertaken, Duval pointed out (on a basis of a material of 21 cases of malignant retroperitoneal tumours confirmed by explorative biopsy and biopsy) that radiation therapy should be the treatment of choice and the only treatment in cases of malignant lymphomata, which are very radiosensitive, the main reason being the high mortality associated with operation for such tumours.

Pack & Tabah, who are of the same opinion, present the indications for radiotherapy for retroperitoneal tumours thus: 1. Inoperable retroperitoneal tumours. 2. Recurrence after operation. 3. Cases in which a fraction of the tumour had to be left in situ on account of infiltration of a vital organ (in this instance marking of the site with a small silver clip is recommended so that the post-operative radiotherapy can be exact as possible). 4. Malignant lymphomata (when early very localized cases are excluded, radiotherapy is preferable rather than attempts at radical operation). 5. As a post-operative supplement in many cases of malignant retroperitoneal tumour.

COURSE AND PROGNOSIS

While simple retroperitoneal cysts, when correctly treated, have, as a rule, good prognoses, it is apparent from the above that it is difficult to express an opinion regarding the prognosis for other retroperitoneal tumours concerning which Fleischer-Hansen writes that "they are on the borderline between good and evil".

On the one hand, a "benign" retroperitoneal tumour which has run a benign course for many years may suddenly threaten the patient's life on account of malignant degeneration or the prognosis may deteriorate on account of recurrences which tend to be repeated and which may also occur after operative removal of benign retroperitoneal tumours.

On the other hand, the malignant retroperitoneal tumours which, in the majority of cases, have a very serious prognosis (average duration of life after operation is nine months (44)), may occasionally run a surprisingly favourable course. In this connection Pack & Tabah record three cases of inoperable sarcomata: a liposarcoma, an unclassifiable sarcoma and a lymphosarcoma which survived for > 5 years, > 8 years and > 13 years, respectively, after radiotherapy (the last mentioned patient was without recurrences after the 13 years but could not be traced longer). Duval recorded, similarly, three inoperable cases which, following explorative laparotomy (without biopsy) and radiotherapy, have survived seven, eight and ten years, to date. On account of the pronounced radiosensitivity, Du-

val presumed that lymphosarcomata must have been concerned.

The incidence of metastases is varyingly reported. Donnelly and Andrews state that spread to the lungs, vertebrae, liver or regional lymph glands is found in 30-33 per cent of the cases but the majority of authors state that metastases occur both rarely and late (1, 7, 21).

MATERIAL

The material consists of 11 cases of retroperitoneal tumours all of which were verified at operation. These comprise 2 cysts, 1 haemangiofibroma, 2 reticulo- or lymphosarcomata, 4 other sarcomata, 1 tumour which was difficult to classify and one case in which biopsy was not undertaken.

The two malignant lymphomata manifested themselves as definitely localized abdominal tumours when the patients came for treatment so that these cases undoubtedly fall within the definition employed. While the remaining tumours classified histologically will, of course, be included, the wisdom of including the case without microscopic diagnosis is debatable. It was, however, considered to be of interest particularly when the course proved to be surprisingly favourable.

When the absence of tumours derived from adipose tissue and the occurrence of the rare haemangioma are excluded, the composition of the material is, by and large, typical and corresponds to that found in other materials.

The retroperitoneal haemangioma (or haemangiofibroma) is a condition which has very rarely been described. According to Newman & White it has only been described previously on four occasions in the international literature: Hilse (16) 1928, Harris (15) 1929, Millmann (29) 1924 and Newmann & White (33) 1958. It is difficult to express an opinion regarding the prognosis of these retroperitoneal haemangiomas on account of the limited material but apart from the case described by Hilse, they appear to have been benign. The author's case also ran a benign course. The case history will be reviewed briefly:

III. The patient was a female aged 26 years. In 1952 laparotomy with ventral fixation of the uterus was undertaken. On that occasion, no sign of tumour in the abdomen was observed.

Six months later, the patient was admitted to a medical ward having experienced pain in the upper part of the abdomen. The pain was continual but with periodic exacerbations. Simultaneously, bile-stained vomiting and clay coloured diarrhoea developed. The urine was normal in colour. A markedly tender swelling under the right costal margin was demonstrated and the patient was transferred to Department V with the diagnosis of cholecystitis.

On admission, the patient was in pain and subfebrile. No jaundice was present. The symptoms sub-

Table 2.

The Commonest Subjective Symptoms and Objective Findings in the Cases of Primary Retroperitoneal Tumour.

Number	Tumour	Age Sex	Duration of Symptoms (Months)	Dyspepsia	Abdominal Pain	Loss of Weight	Pyrexia	Palpable Tumour	Haemoglobin %	ESR mm	Haematuria	Urography	x-Ray of Stomach	x-Ray of Colon
I	Cyst	47 F	3-4	+	+	-	-	+	78	17	-	Normal		Colitis
II	Cyst	45 F	12	+	+	-	-	+	93	5	-			
III	Fibrohaem- angioma	26 F	3	+	+	-	-	+	91	9	-		Normal	Normal
VI	Malignant Lymphoma	65 M	12	+	-	+	+	+	67	106	-	Dislocation Abn. Excret	Normal	Dislocation
V	Malignant Lymphoma	35 M	2	+	-	-	-	+	113	104	-	Dislocation	Dislocation	Dislocation
VI	Sarcoma	12 M	1	+	+	-	+	±	96	30	+	Abn. Excret	Dislocation	
VII	Sarcoma	49 F	6	-	+	-	+	+	95	47	+	Abn. Excret		Dislocation
VIII	Sarcoma	59 M	9	+	+	+	-	+	86	106	-	Normal		Dislocation Colitis
IX	Sarcoma	4 F	6	+	+	+	-	+	87*	19*	-*	(Normal)*		Elongated sigmoid colon
X	Type ?	6 M	-	-	+°	-	-	+	83	20	+	Normal	Dislocation	Dislocation
XI	No Biopsy	36 M	2	+	+	+	-		89	39 45	-	Abn. Excret	Normal	Perisigmoiditis

*) After radiotherapy. °) After trauma.

sided after 4-5 days but quite a firm, transverse, sausage-shaped swelling persisted in the right side of the epigastrium.

Investigations: Hb: 91 per cent, ESR 9 mm. Microscopic examination of the urine: normal. Blood urea: 22 mg, Icteric index: 7, Diastase < 150 × 4, Urobilin and bile pigment: negative × 4, Faeces: (+), --, --, Benzidine, B. P. 110/80. X-ray examination of the stomach, cholecystography and X-ray of the thorax: normal.

No definite diagnosis could be established. At laparotomy a large irregular, bluish black tumour mass was found, the surface of which was covered with numerous grape-like excrescences which contained altered blood. The tumour, which displaced the pylorus and the duodenum anteriorly, was situated in the position of the head of the pancreas (posterior to normal pancreatic tissue). It was very adherent to the duodenum, extending slightly to the left up the vertebral column to slightly below the pancreas and right up into the hepato-duodenal ligament. The kidneys and the liver were normal. Radical operation was impossible.

Microscopic examination of the biopsy specimen revealed fibrillary connective tissue with numerous vessels and numerous very large vascular lumina containing blood. There were no signs of specific in-

flammation nor malignancy. Fibrohaemangioma cavernosum.

The patient was submitted to post-operative radiation therapy (6,000 r). The tumour diminished considerably in size and later was no longer palpable.

During the subsequent seven years the patient was admitted to the department on several occasions for various reasons including suspected gastric ulcer (no ulcer was demonstrated) and for operation for a diffuse colloid goitre. During this period, the patient was x-rayed on several occasions (measurement of the pancreas, intestinal follow-through and cholecystography). On two occasions the retroventricular space was found to be normal. There have been no clinical indications of recurrence (last examination, October 1959).

The patients in this material do not appear to show any characteristic age distribution.

Out of the 11 tumours, six were in males and five in females. Sarcomata dominated in males while both of the cysts were found in females.

The duration of the symptoms until the patients came for treatment averaged five months and the maximum time was a year (in a case of malignant lymphoma). Three of the patients were

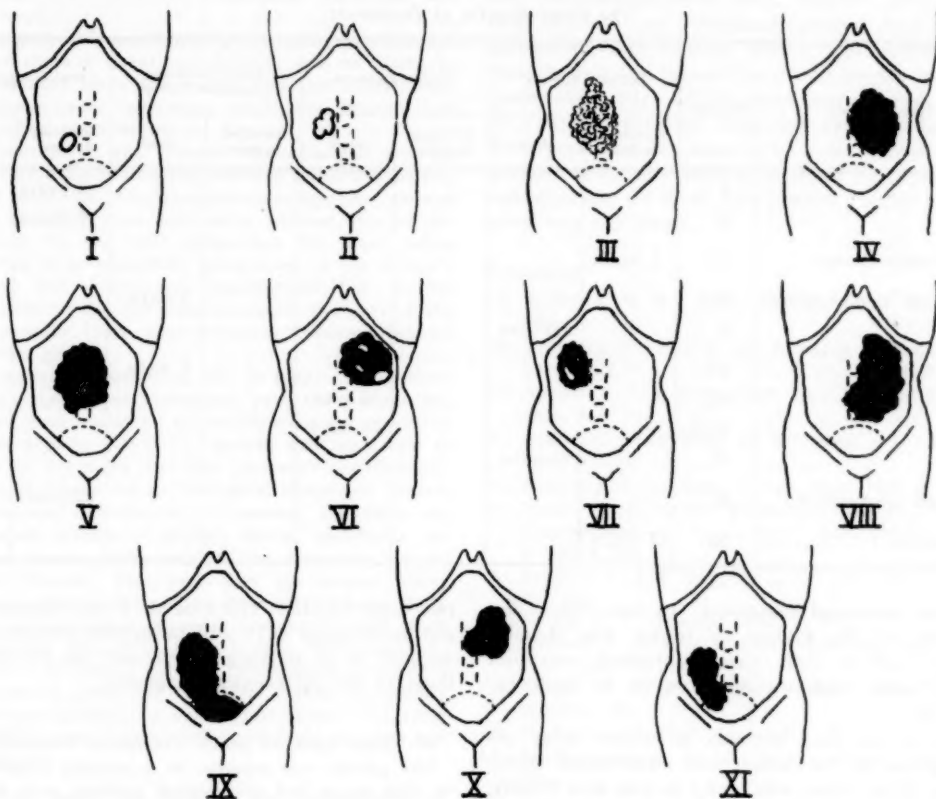


Fig. 1.
Localization of the Tumours.

admitted as emergencies under the diagnosis of cholecystitis (III), acute abdomen (VI) and suspected intra-abdominal haemorrhage (X). In the first two of these cases infection had probably occurred and in the third case haemorrhage into the tumour of traumatic origin had probably taken place.

The most frequent subjective symptoms were dyspepsia and abdominal pain. These symptoms were present in nine and eight, respectively, out of the 11 patients at the time they came for treatment. None of the patients had experienced pain in the back or loins. Four patients had noticed loss of weight and three had had more or less pronounced constipation. Three patients, all of whom had malignant tumours, had experienced uncharacteristic prolonged pyrexia for shorter or longer periods. One patient (VIII) sought medical advice on account of increasing abdominal circumference. In one patient oedema of the legs gradually developed (VII) and another developed symptoms of medullary compression late in the course of the disease (V). Apart from slight pollakiuria in an isolated patient (VI) no subjective urological complaints were present.

On admission, a palpable abdominal tumour was found in all of the patients with one exception (VII) (Figure 1). In an isolated patient the tumour could be felt on rectal exploration (IX). In no case was ascites demonstrated.

While the ESR in the group of patients with benign tumours was normal or only slightly raised, considerably high and rising ESRs were found in the patients with malignant tumours. The haemoglobin percentage did not provide any information of value but a falling percentage was found in four of the patients with malignant tumours. In one patient macroscopic haematuria was demonstrated (VI) and in two further patients microscopic haematuria was present (VII and X). In the five cases in which the blood urea was estimated (III, IV, V, VII, VIII), no reduction of renal function of any consequence was found. No clinical signs of hypoglycaemia which initiated blood sugar estimations was observed in any of the patients. Nothing is recorded concerning differences in temperature between the lower limbs.

Intravenous urography was undertaken pre-operatively in eight of the patients. Five of these

Table 3.
The Final Results of Treatment.

Type of Tumour	Number	Radiation Therapy		Partial Extirpation		Partial Extirpation + Radiation Therapy		Total Extirpation	
		Surviving No recur.	Dead	Surviving No recur.	Dead	Surviving No recur.	Dead	Surviving No recur.	Dead
Cysts	I							4 years	
	II							17 years	
Fibrohaemangioma	III	7 years							
Malignant Lymphomata	IV						5 days		
	V		2½ yrs.						
Other Sarcoma	VI						9 mths.		
	VII			5 wks.					
	VIII			13 days					
	IX		6 mths.						
Difficult to Classify ..	X							22 years	
No Biopsy	XI	17 years							

showed abnormal urograms: In two cases dislocation of the kidney or ureter was demonstrated and in four cases abnormal excretion was present (absence of excretion or hydronephrosis).

Out of the nine patients in whom x-ray investigation of the colon was undertaken, dislocation of the colon was found in five and, finally, dislocation of the stomach was found in three out of the six patients examined. Lateral exposures had only been taken in a minority of cases and there can be no doubt that more frequent employment of this exposure would be of considerable assistance in establishing the correct diagnosis in many cases.

In this present material, the diagnosis if not established with certainty, was mentioned as a possibility in five of the cases. Out of other patients in whom the condition was misdiagnosed as primary retroperitoneal tumour, cases of aortic aneurysm, a large suprarenal tumour and metastases from a tumour of the testis which did not become clinically demonstrable until after laparotomy, were concerned.

All of the patients were treated either operatively, by radiation or by a combination of these methods (Table 4). In three cases radical operation was possible.

The two cases of retroperitoneal cysts both appear to have been cured by extirpation. The tumour which was difficult to classify (X) resembled a sarcoma but was submitted to radical operation and no recurrence has appeared during 22 years. This tumour was probably benign and derived from the primitive kidney. Among the five patients in whom autopsy was performed, metastases to the liver or lungs were found in

two cases (V, IX). The case in which biopsy was not undertaken (XI) will be briefly reviewed on account of its striking course and the considerations in the differential diagnosis:

XI. Male aged 36 years. Previously healthy.

The patient was referred to a medical department in 1942 as he had experienced periodic pain to the right of the umbilicus with varying radiation. The patient stated that he had lost 20 kg in weight in the course of one year. Slight constipation. No urological symptoms.

Investigations: Hb. 89 %, ESR 39—45 mm, BP: 140/90, Mantoux: negative (1/100), Urine: No albumin, blood, pus or sugar. Microscopic examination of the urine: normal, WR: negative, GCFT: negative, Diastase: 32, Friedmann reaction: negative. Intravenous urography: normal conditions on left side. No excretion on right side. X-ray examination of the colon: perisigmoiditis, abdominal tumour (not colic). X-ray examination of stomach: normal.

The patient was then transferred to Department V. The general condition was good. Abdominal examination: A very firm nodular, tender, slightly mobile tumour was felt deeply to the right of the umbilicus. Rectal examination: normal. External genitalia: Tenderness of the right testicle but no palpable abnormality. Left testicle normal. No peripheral glandular enlargement.

The diagnosis was uncertain. An explorative lumbar incision was made and an irregular nodular very hard tumour was found in close relation to the lower pole of the right kidney. The tumour continued over the pelvic brim and was adherent to the peritoneum and the inferior vena cava. The upper part of the right ureter which disappeared into the tumour mass was dilated to the thickness of a pencil. The kidney was somewhat enlarged but with no sign of tumour formation. It was considered that a secondary tumour (from the right testis?) was concerned and the

prognosis was considered to be poor. No biopsy was performed.

The patient was submitted to post-operative radiation therapy (total dose 1,725 r) and, on discharge four months later, the weight and the haemoglobin percentage were increasing while the tumour had diminished considerably in size.

A year later, the patient was admitted for the follow-up examination and renewed radiation therapy (total dose 900 r). Intravenous urography showed rapid excretion from both sides without sign of obstruction. In the right pyelogram the renal pelvis appeared to be somewhat compressed as the distance between the calyces was considerably less on the right than on the left side. Alongside the part of the lumbar spine there were extensive calcium shadows (calcified glands).

Follow-up Examination (24.10.1959): Apart from periodic right-sided abdominal pain the patient has enjoyed good health on the whole since the operation (17 years previously). The patient has been able to attend to his work and has increased satisfactorily in weight. There are no urological symptoms. Moderate periodic constipation is present. Objective examination reveals a slightly tender indefinite resistance in the right side of the abdomen but no definite tumour. The liver does not project under the costal margin. No ascites. External genitalia: Both testes are somewhat atrophic and tender but show no tumours. Hb: 96 %, ESR: 9 mm. Microscopic examination of urine: normal. Intravenous urography: simultaneous punctual excretion giving completely normal pyelograms. No visible metastases. The large calcified glands remain unchanged from the previous photographs.

In this case, the tumour was considered at operation to be malignant and further intervention was, therefore, withheld. The patient reacted well to radiation therapy. The fact that he has been free from recurrence for 17 years probably signifies that the condition is definitely cured. It is impossible to state with certainty what condition was concerned but the original supposition of metastases from a tumour of the testes may be excluded by the favourable course of the disease. The condition was too extensive and radiosensitive to have been "primary retroperitoneal fibrosis". The very considerable loss of weight and the high ESR make it appear improbable that a benign, radiosensitive tumour was concerned. There was no evidence to suggest Hodgkin's disease or other systemic disease. Enlarged tuberculous glands are a possibility but the negative Mantoux reaction does not support this theory. Finally, a radiosensitive sarcoma may have been concerned in which the course was surprisingly favourable (cf. the case of lymphosarcoma described by Pack & Tabah which was without recurrence 13 years after radiotherapy).

SUMMARY

The literature on primary retroperitoneal tumours is reviewed.

Eleven cases of retroperitoneal tumour are reported among which are a rare case of cavern-

ous fibrohaemangioma and, further, two cysts, two reticulo- or lymphosarcomata, four other sarcomata, one tumour which was difficult to classify and one tumour in which biopsy was not undertaken. Five of the cases were cured, three by radical operation and two by radiotherapy. The remaining six cases which were treated by partial extirpation with or without post-operative radiotherapy all died. The longest period of survival was 2½ years.

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TRAUMATIC ATRESIA OF THE UTERUS

By CHRISTINE KÆSTEL and JØRGEN ERIKSEN

DEFINITION

By the term traumatic atresia of the uterus is understood partial or complete obliteration of the cavity of the uterus, occurring most frequently after curettage.

This clinical condition has also been described by the following terms: Synécchies utérines, insuffisances menstruelles traumatiques, traumatic intrauterine adhesions, amenorrhoea traumatica and agglutinatatio uteri.

HISTORY

The condition was first described by Fritsch (8) in 1894.

A woman aged 25 years consulted Fritsch on account of sterility. Twenty four days after her first delivery two years previously curettage had been undertaken on account of post partum haemorrhage, and since then no menstruation had occurred. Fritsch found a small firm uterus into which it proved impossible to introduce the finest sound. With a scalpel and dilator, he fashioned a cavity 7 cm. in length in the uterus and introduced a laminaria tent. A fortnight later, the artificial cavity had closed again and no menstruation occurred.

In the subsequent thirty or more years, only about ten cases of atresia were published and among these the first case to be described of cervical atresia with haematometra (11). In 1927, Bass (4) published a communication concerning 20 cases of atresia which had developed following therapeutic abortion produced by curettage. During the following 20 years only reports of isolated cases were published (12, 17, 35, 38, 39, 40). In 1946, Stamer (36) collected 38 cases from the literature and published further 24 cases of his own collected over a period of a few years. Thereafter, several papers were published concerning materials of more or less similar extent. Hald (13) was the first to draw attention to the characteristic hysterosalpingo-

gram. The name of Asherman (1, 2, 3) was, however, the first to be associated with the clinical picture. In numerous excellent studies, Asherman published reports of numerous cases of traumatic atresia of the uterus (by 1953, he had published a total of 120 cases) and he was the first to draw attention to the reduced fertility of these patients, also after treatment. Similarly, Asherman emphasized the significance of employment of the hysterosalpingogram to establish an exact diagnosis. In recent years, numerous French authors have shown interest for the condition and its treatment, *e. g.*, Netter, Musset, Lambert and Salomon (23, 24, 25, 27, 28, 29, 30, 31, 33).

ETIOLOGY

Various possible causes for the development of the condition have been mentioned in the literature. Among these are: hot intrauterine douches, chemical and electric cauterization, and packing. There is, however, no doubt that nowadays curettage, primarily of a uterus which has undergone changes of pregnancy, is the cause of atresia. In the present material which comprises 61 cases, atresia developed in all of the patients following curettage.

In these cases curettage was undertaken on account of:

- | | |
|---|----------|
| 1) Post partum metrorrhagia (within 2 months) | 51 cases |
| 2) Missed abortion | 3 " |
| 3) Simple abortion | 2 " |
| 4) Therapeutic abortion | 2 " |
| 5) Haemorrhage from non-pregnant uterus | 3 " |

Total.... 61 cases

Re 1) The group of post partum metrorrhagia constitutes such a great proportion of this material because the authors have undertaken a follow-up investigation of patients treated for post partum metrorrhagia by curettage (Cf. p. 50). This investigation revealed 33 out of the 51 cases.

From: The Department of Gynaecology, The Copenhagen County Hospital in Gentofte. (Head: Valdemar Madsen).

Re 2) Two of these patients were primigravidae and the third had been treated on two previous occasions by curettage on account of post partum metrorrhagia. In this case, it is possible that the atresia had developed previously and was the reason for the missed abortion.

Re 3) One of the patients was a primigravida in whom curettage was undertaken on account of abortion in the second month while the other was pregnant for the fourth time and had undergone three normal deliveries, aborted in the third month and was treated with curettage and again six months later on account of metrorrhagia.

Re 4) The first patient had three normal deliveries with no curettage in connection with them. An abortion between the first and second deliveries was treated with curettage. Following the last delivery, therapeutic abortion was undertaken twice at an interval of a year, re-evacuation being necessary on one occasion.

The second patient had had one normal delivery, curettage on three occasions and therapeutic abortion twice.

Re 5) The first patient had never been pregnant. Curettage had been undertaken on two occasions with an interval of a year. The second patient had been subjected to curettage on seven occasions between her 18th and 23rd years.

The third patient was subjected to curettage of the uterine mucosa for the first time at the age of 15 years. From her 20th to 23rd years she had been subjected to curettage on a total of 10 occasions, *i.e.*, practically every third month.

PATHOGENESIS

Investigation of the uteri removed from cases of atresia confirmed the results obtained by other authors (Netter et al. 31). As a rule, greater or lesser cavities were found in a rather small firm uterus. On microscopic examination, the cavities were found to be lined with endometrium, frequently of atrophic type and, occasionally, haemosiderophages were observed. In cases in which the uterine cavity was obliterated, the tissue was found to consist of smooth musculature and connective tissue.

Werth (43) in 1895 examined six uteri removed from 3—16 days after curettage and found that the effect of the curettage was very heterogeneous at various different parts of the cavity. The changes varied from quite unaffected regions to region where both the basal stratum of the mucosa and the myometrium were injured. In the latter regions, granulation tissue was still present 16 days after the curettage while the remainder of the cavity was lined with endometrium.

On this basis it seems reasonable to presume that atresia of the cavity develops where parts of the cavity opposite one another with injured or denuded myometrium develop granulation tissue and form bridges which later become infiltrated with musculature and connective tissue.

SYMPTOMATOLOGY

Traumatic atresia of the uterus is characterized primarily by amenorrhoea or hypomenorrhoea. In a series of cases, this was the only symptom. In addition, some of the patients experienced low abdominal pain of more or less cyclic character. In some patients the main complaint was only sterility but, as a rule, it appeared that hypomenorrhoea had been present simultaneously. During the past seven years it has also been apparent that very frequently in these patients with traumatic atresia of the uterus, if they should become pregnant, complications in the form of haemorrhage, abortion, missed abortion, premature delivery, placenta accreta or extensive insertion of the placenta with placenta praevia may occur.

DIAGNOSIS

Traumatic atresia of the uterus should be suspected when amenorrhoea or hypomenorrhoea develops in a patient following curettage. Apart from this, the patient feels perfectly well and does not present any signs of endocrine disturbance. As a rule, no abnormality is revealed by gynaecological examination but the uterus is frequently smaller than normal. Cases have been described in the literature in which the uterus was enlarged on account of haematometra (11, 19, 36, 45) but no such cases were encountered in the present material.

The suspicion may be confirmed by sounding but frequently even the finest sound cannot be introduced. It is necessary to undertake hysterosalpingography in order to verify the diagnosis and to determine the extent of the changes.

The characteristic finding on hysterosalpingography is the absence of, or defective filling of, the uterine cavity. The filling defects may assume all possible forms and they are frequently irregular but always sharply delimited and completely homogeneous. The filling defects are uniform in all exposures and are independent of the quantity of radio-opaque medium injected. Injection of the radio-opaque medium into the myometrium is not infrequently observed.

Many authors differentiate between total and partial atresia of the uterus and divide the latter into cervico-isthmic atresia and corporal atresia. This sub-division is of little practical significance as the partial atresia of the corpus is the most frequent, total atresia is very rare and cervico-isthmic atresia is frequently combined with changes in the body of the uterus.



Fig. 1.



Fig. 2.

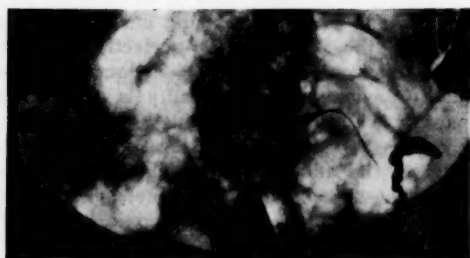


Fig. 3.

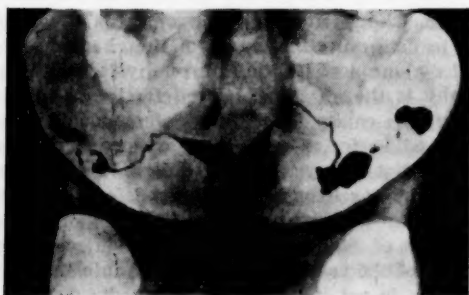


Fig. 4.

Figures 1—4 show various examples of partial atresia.

TREATMENT

The object of treatment is to restore normal uterine function both as regards menstruation

and as regards nidation and the ability to sustain pregnancy and delivery.

It was previously believed that the patient was cured if menstruation occurred after treatment but since the publication of Asherman's works (2, 3) it has become obvious that a number of the patients do become pregnant after treatment but many of these pregnancies do not go to term and the delivery is frequently complicated.

An essential condition for successful dilatation therapy is that a sufficient quantity of normally functioning endometrium remains. Although the picture obtained by hysterosalpingography reveals quite a large cavity, the endometrium is not necessarily normal. One of the patients in the present series (No. 6 in Table 1) had a practically normal cavity after treatment but amenorrhoea persisted and on hysterectomy the entire endometrium was found to be low atrophic.

The treatment of atresia has undergone few changes since Fritsch undertook dilatation. Dilatation may be undertaken per vaginam by Hegar's method possibly combined with the introduction of laminaria tents, or abdominally by means of hysterotomy in which an attempt is made to reconstruct a cavity either manually or instrumentally. As a substitute for the absent endometrium, Strassman (38, 39, 40) suggested a method by which one of the ovarian tubes is introduced through the newly-formed cavity into the vagina. Strassman stated that he has observed normal pregnancy following this treatment. In recent years, great interest has been evoked by communications, particularly from French sources, concerning successful results of endometrial transplantation (23, 29, 31) but inadequate information is available concerning the late results of this procedure.

Out of the 61 patients in this material, five were treated in other departments, 27 were not treated and 29 were treated in this department according to the following principles: Following an examination for orientation in which the uterus was sounded or an attempt was made to sound the uterus, a hysterosalpingogram was, as a rule, carried out. Thereafter, dilatation was undertaken either by Hegar's method alone or supplemented by the introduction of laminaria tents. Occasionally the intervention was undertaken in two seances. In the majority of cases dilatation to Hegar no. 10 or more was undertaken.

As a rule, the patients received penicillin pre-operatively and for the five succeeding days. In nine cases, the treatment was repeated because menstruation and the hysterosalpingogram had not improved 3—6 months later.

During treatment of these 29 patients, the uterine wall was thought to have been perforated in two cases. No peritoneal reactions were observed following immediate interruption of the intervention and institution of conservative ther-

Table 1.

Patient No.	Age on Treatment	Before Treatment			After Treatment				
		Menstrual Condition	Hysterosalpingographic Changes	No. of Deliveries	Menstrual Condition	Hysterosalpingographic Changes	Pregnancy desired	Pregnancy Occurred	Period of Observation Years
1	23	amenorrhoea	pronounced	1	unchanged	unchanged	yes	no	3
2	33	amenorrhoea	pronounced	2	unchanged	unchanged	no	no	($\frac{1}{2}$)*
3	27	amenorrhoea	pronounced	2	unchanged	unchanged	no	no	2
4	35	amenorrhoea	pronounced	0	unchanged	unchanged	yes	no	1 $\frac{1}{4}$
5	29	amenorrhoea	pronounced	0	much better	much better	yes	no	2
6	33	amenorrhoea	pronounced	0	unchanged	much better	yes	no	2 $\frac{1}{2}$
7	38	amenorrhoea	pronounced	3	slightly better	unchanged	no	no	4
8	19	amenorrhoea	cervical atresia	1	slightly better	slightly better	yes	no	1 $\frac{1}{2}$
9	24	amenorrhoea	cervical atresia	2	unchanged	slightly better	yes	no	1
10	32	amenorrhoea	cervical atresia	0	unchanged	unchanged	yes	no	1 $\frac{1}{2}$
11	34	amenorrhoea	cervical atresia	2	normalized	much better	no	no	1 $\frac{1}{2}$
12	34	amenorrhoea	cervical atresia	3	unchanged	—	no	no	2 $\frac{1}{4}$
13	19	amenorrhoea	cervical atresia	1	unchanged	—	no	no	2 $\frac{1}{4}$
14	30	amenorrhoea	cervical atresia	1	unchanged	—	no	no	2 $\frac{1}{4}$
15	27	amenorrhoea	moderate	3	unchanged	—	yes	no	1 $\frac{1}{4}$
16	25	amenorrhoea	—	2	slightly better	pronounced	no	no	1 $\frac{1}{4}$
17	26	amenorrhoea	—	4	slightly better	moderate	yes	yes	1 $\frac{1}{4}$
18	27	amenorrhoea	—	2	unchanged	pronounced	no	yes	2
19	22	amenorrhoea	—	1	slightly better	—	yes	yes	2 $\frac{1}{4}$
20	24	amenorrhoea	—	1	slightly better	—	yes	yes	2 $\frac{1}{2}$
21	23	amenorrhoea	—	1	much better	—	yes	yes	($\frac{1}{2}$)*
22	24	amenorrhoea	—	3	normalized	—	yes	yes	1 $\frac{1}{4}$
23	28	severe hypomenorrhoea	pronounced	1	slightly better	much better	yes	yes	1 $\frac{1}{2}$
24	34	severe hypomenorrhoea	pronounced	1	unchanged	much better	yes	no	3 $\frac{1}{2}$
25	34	severe hypomenorrhoea	—	2	unchanged	pronounced	yes	yes	3 $\frac{1}{2}$
26	29	severe hypomenorrhoea	—	1	slightly better	moderate	no	no	2 $\frac{1}{4}$
27	25	slight hypomenorrhoea	moderate	1	normalized	unchanged	yes	no	1 $\frac{1}{4}$
28	28	slight hypomenorrhoea	pronounced	1	unchanged	normalized	yes	no	1
29	29	normal	pronounced	0	unchanged	normalized	yes	no	3 $\frac{1}{2}$

*) After this period of observation these patients were subjected to hysterectomy.

apy. Seven patients showed brief pyrexia in connection with the intervention but, with these exceptions, no complications were observed.

Particulars of all of the patients subjected to treatment are recorded in Table 1.

As appears from the Table, the patients with amenorrhoea comprise by far the largest group,

viz. 22. Out of these, six had monthly haemorrhage consisting of a few drops. The remaining seven patients had varying degrees of reduced menstruation and an isolated patient stated that menstruation was normal.

Hysterosalpingography was undertaken prior to treatment in 20 patients. The seven patients

characterized by cervical atresia in the Table showed filling of the cervical canal only on hysterosalpingography and it is, therefore, impossible to express any opinion concerning possible changes higher up in the uterine cavity. In 11 patients the uterine cavities were small and grossly changed and two patients had less extensive changes.

Finally, in an attempt to estimate the fertility of the patients prior to the development of the atresia, the number of previous pregnancies is recorded.

In comparing the state of menstruation before and after treatment, the authors made strict requirements, as definite and prolonged improvement of the quantity and duration of menstruation was required, in order to term the conditions as "slightly better" or "much better."

In a similar manner, in evaluating the picture obtained on hysterosalpingography, the authors required considerable difference before the results were designated as better.

RESULTS

Menstruation: As only "much better" and "normalized" are regarded as satisfactory, it appears that this result has been obtained in only five out of the 29 cases. The remaining 24 cases must be regarded as unsatisfactory.

Hysterosalpingography: This examination was undertaken in 21 patients after treatment. In two patients the picture was normalized and in five it was greatly improved (all seven patients had shown extensive changes prior to treatment). Two patients showed moderate changes but hysterosalpingography had not been undertaken prior to treatment. Thus, at least seven (possibly nine) cases, as judged from the hysterosalpingogram, may be termed satisfactory.

Fertility: Nineteen of the patients expressed a genuine desire to become pregnant. Of these, 12 remained sterile following an average period of observation of approximately two years. The remaining seven patients became pregnant. The course of these pregnancies was, however, so remarkable that each will briefly be accounted for:

- Patient No. 17: Normal delivery, large biplacenta living infant weighing 4,500 g.
- Patient No. 19: Delivery. Despite persistent attempts no further information could be obtained.
- Patient No. 20: Missed abortion.
- Patient No. 21: Abortion in fourth month with placenta accreta. Emergency hysterectomy was performed on vital indications.
- Patient No. 22: Premature delivery, placenta accreta, living infant weighing 2,200 g.
- Patient No. 23: Premature delivery, living infant weighing 1,750 g.

Patient No. 25: Placenta praevia with very extensive insertion. For this reason Caesarean section and hysterectomy were undertaken. Living infant weighing 2,000 g.

It will be observed that out of 19 patients desiring pregnancy, this occurred in seven cases and only in one (or at the most two) did this proceed normally.

DISCUSSION

The present work confirms the impression previously gained that traumatic atresia of the uterus is not a particularly rare condition. Further, it reveals that the results of treatment are extremely unsatisfactory. It is difficult to compare the results of the different works on the subject, first and foremost because information concerning menstruation is very subjective and also because the picture obtained by hysterosalpingography and the fertility have first been included in the evaluation of the result of treatment in recent years. The authors are aware that the present results appear poorer than those of the majority of other authors but, on the other hand, they have been unable to find any other directly comparable work.

The authors have accounted for the result of pure dilatation therapy performed per vaginam. The authors have no experience of abdominal dilatation but even if a better impression of the uterine cavity may possibly be obtained, they do not consider that the advantages are so great that they justify the major intervention. The poor results of dilatation per vaginam are undoubtedly due to the fact that the cavity is reconstructed by means of dilatation but it does not prove possible to line it with functioning endometrium. The extent to which hormone therapy in connection with dilatation could have improved upon these results is still unknown as such therapy was only attempted in isolated cases. The authors do not consider that the results of treatment can be improved considerably unless it proves possible to reline the uterine cavity with functioning endometrium. Communications concerning endometrial grafting are still few and uncertain.

The authors have treated and followed-up these patients and have observed the uncertain results and have arrived at the conclusion that until better treatment is available, treatment should be reserved for patients who have been orientated concerning the nature of the condition and the limited possibilities of cure and who, nevertheless, desire intervention. The authors consider that by not advising treatment and instead persuading the patient to accept the condition, a series of patients have been spared considerable psychic trauma on account of disappointed hopes.

Great weight must, therefore, be laid upon the possibilities for preventing the development of

this condition. According to the authors' experience traumatic atresia of the uterus develops in the majority of cases following curettage on account of post partum metrorrhagia. The prophylaxis, therefore, begins at delivery where correct post partum treatment directed towards avoiding retention of placental tissue should be undertaken. The placenta should be carefully inspected to ascertain that it is complete and in doubtful cases intrauterine palpation must be undertaken. If a patient develops post partum haemorrhage greatest restraint should be exercised and the condition should be treated conservatively as far as possible, *i. e.*, with oestrogenic hormones, oxytocic preparations and blood transfusion, most particularly when microscopic examination of the tissue removed in a number of cases does not reveal remnants of placental tissue (See next article).

If curettage cannot be avoided, it is obvious that this must be undertaken very carefully and that in all cases oxytocic preparations should be administered in connection with the intervention. A sharp curette should only exceptionally be employed.

SUMMARY

Sixty one cases of traumatic atresia of the uterus are presented. Total or partial obliteration of the uterine cavity had developed in 51 of the cases following curettage in the first two months after a delivery. The pathogenesis and symptoms are discussed. It is emphasized that curettage of the pregnant or recently pregnant uterus followed by amenorrhoea, hypomenorrhoea or sterility in an otherwise healthy woman should arouse suspicion of atresia. The characteristic hysterosalpingogram is described. Treatment with dilatation according to Hegar's method, and as a rule, with the insertion of laminaria, was undertaken in 29 patients. The results of treatment are given for each individual patient. In only five patients did the treatment result in normal or practically normal menstruation. No relation could be found between the size of the uterine cavity as shown by hysterosalpingography and the extent of menstruation. The treatment was also evaluated by the fertility during a period of observation of an average of two years. Out of 19 patients who desired pregnancy, only seven became pregnant within the period of observation. Five of these pregnancies ran pathological courses.

On account of the unsatisfactory results, the authors advise that conservatism should be exercised as regards treatment unless better methods become available. Further, the significance of prophylaxis is emphasized: Correct post partum treatment, meticulous examination of the placenta and intrauterine palpation in doubtful cases. Curettage within the first two months after delivery should not be undertaken until other treatment has been attempted and then with great care.

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THE INCIDENCE OF UTERINE ATRESIA AFTER POST-PARTUM CURETTAGE

A FOLLOW-UP EXAMINATION OF 141 PATIENTS

By JØRGEN ERIKSEN and CHRISTINE KÆSTEL

During a short period, several cases of traumatic atresia of the uterus were encountered in this Department. These cases had developed following curettage for post partum metrorrhagia and it was therefore considered desirable to investigate the incidence of traumatic atresia of the uterus following this treatment.

During the period Aug. 1. 1953 to Jan. 1. 1956, a total of 141 patients were submitted to curettage within two months after delivery. Questionnaires were sent to these patients, at least one year after the treatment, in which information concerning the quantity, duration and frequency of menstruation was sought. All of the questionnaires were answered.

Forty five patients stated that menstruation had ceased or diminished in quantity and/or duration following the curettage. An attempt was made to summon these patients for interview and gynaecological examination with uterine sounding and, if possible, hysterosalpingography.

Five patients had moved out of reach and it proved impossible to summon four for examination. Out of the 36 patients who were thus submitted to examination, traumatic atresia of the uterus was found in 33. In 27, the diagnosis was verified by out-patient hysterosalpingography and the remaining six had amenorrhoea and complete closure of the cervical canal, this latter being confirmed by sounding. It thus appears that at least 33 patients out of 141, *i. e.*, 23.4 per cent had developed traumatic atresia of the uterus. When the nine patients not examined are also considered and concerning whom the information available is very suspicious, it appears that at least $\frac{1}{4}$ of all the patients treated with curettage following post partum metrorrhagia developed traumatic atresia of the uterus.

Apart from the communication by Asherman concerning five cases of atresia of the uterus which developed among 13 patients treated with curettage on account of post partum metrorrhagia, the authors have not been able to find any similar accounts. The fact that the incidence in this material is much greater than generally assumed is due, among other factors, to the diagnosis not being generally recognized and for this reason numerous patients are

treated under other diagnoses and others do not seek medical advice at all. Out of the patients questioned in this series, 25 had experienced

Table 1.
Material Subdivided According to Time of Treatment
in Relation to Delivery.

Time	No. Patients Treated	Cases of Atresia Found	Percentage Incidence
1st. Week	9	0	0
2nd. Week	47	17	Total 26 Approx. 33
3rd. Week	21	6	
4th. Week	10	3	
5th. Week	19	4	
6th. Week	11	1	Total 7 Approx. 17
7th. Week	11	2	
8th. Week	13	0	

amenorrhoea for more than one year without any further investigation being initiated.

Analysis of the material reveals (Table 1) that the greatest risk of development of atresia of the uterus is present if curettage is undertaken during the second, third or fourth weeks after delivery, as $\frac{1}{3}$ of these patients develop traumatic atresia of the uterus. In the first week after delivery, nine patients were submitted to curettage and none of these developed traumatic atresia of the uterus, an observation which appears noteworthy. The incidence of atresia fell again when curettage was undertaken after the fourth week.

Among the 141 patients there were five in whom curettage was undertaken on two occasions at intervals of 1-8 days. Four of these patients developed atresia while the fifth had normal menstruation and normal hysterosalpingography.

Microscopic examination of the curettings was undertaken in 85 out of the 141 cases. Microscopic examination was performed particularly in view of the presence of placental tissue. This was found to be present in only 29 cases. In 33 cases, myometrium was said to be present and in 12 of these "very plentiful myometrium" was reported. Out of these 12 cases alone, five cases of atresia occurred. No difference in the incidence of traumatic atresia of the uterus was

observed among the 21 cases in which myometrium was encountered and in the 52 cases in which no information on this subject was available.

It must be presumed that it is less easy to injure the myometrium in the contracted uterus and, for this reason, the majority of gynaecologists agree that oxytocic preparations should be administered in connection with curettage. This rule has been observed in this Department. Similarly, whenever this proved possible, a blunt curette was employed.

The question whether infection of the contents of the uterus is of significance for the development of atresia is illustrated by dividing the patients into two groups: An afebrile group comprising 112 patients and a group of 29 patients in whom temperatures of over 38° C were recorded in connection with the curettage. Out of the 112 patients, 24 developed atresia and out of the 29 patients nine patients developed atresia. From these limited figures it is not possible to make any definite deductions but it appears as if infection of the uterine contents increases the risk of the development of atresia.

CONCLUSION

As placental tissue was encountered in only approximately $\frac{1}{3}$ of the curettings submitted to microscopic examination and as atresia developed in approximately $\frac{1}{4}$ of the patients after curettage on account of post partum metrorrhagia

presented here, the conclusion is drawn that curettage should only be undertaken in cases of severe haemorrhage. Oxytocic preparations, oestrogenic hormones, rest in bed and possibly blood transfusion should first be attempted.

SUMMARY

In The Department of Gynaecology, The Copenhagen County Hospital in Gentofte, follow-up examination among 141 patients in whom curettage was undertaken on account of post partum metrorrhagia, revealed 33 cases of traumatic atresia of the uterus. It appears that the incidence is greatest in patients submitted to curettage in the first to fourth weeks after delivery. Out of five patients in whom the intervention was undertaken on two occasions, atresia developed in four. In cases where microscopic examination of the curettings showed the presence of plentiful myometrium, a higher incidence of atresia was found. It is emphasized that only in $\frac{1}{3}$ of the curettings examined microscopically was placental tissue found, and for this reason it is concluded that the greater risk of causing traumatic atresia of the uterus in these patients should cause restraint to be exercised in the employment of curettage as the standard treatment in cases of post partum metrorrhagia.

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General Press Discussion not Desirable.

INTERRUPTION OF PREGNANCY BY INTRAUTERINE INSTILLATION OF SALINE

By HANS SVANE

During recent years, several communications have appeared concerning the employment of saline in cases of ineffective labour pains and for the induction of labour. Aburel et al. (1) employed a 20—35 per cent solution of sodium chloride which was introduced between the membranes and the lower segment of the uterus. For this purpose, they introduced a Nélaton catheter through the cervical canal and injected saline at the rate of 50 drops per minute. The usual quantity was 300 ml but in isolated cases more was employed. In this manner attempts were made to induce delivery in 31 cases and

30 of these women were delivered after an average of 20 hours. All of the infants survived.

Administered intramuscularly, saline also exerts a stimulating effect on labour pains (2, 3). For the induction of abortion hypertonic sodium chloride solution has been employed by Cioc (4) and by Stamm et al. (5) among others. The method employed by these authors consisted of puncture above the symphysis, withdrawal of amniotic fluid and replacement with saline as recommended by Aburel in 1938 (6).

In our Department, saline introduced extra-ovularly into the uterus has been employed for the induction of abortion for more than a year. The method does not appear to have been employed previously according to review of the literature and, as it has yielded good results, the

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author considers it of interest to publish the experience gained.

MATERIAL

The material comprises all cases of therapeutic abortion undertaken in this Department from November 1958 till December 1959. The saline method was employed in all cases irrespective of the duration of pregnancy and the disease for which the abortion was undertaken. The material consists of 100 therapeutic abortions undertaken upon 99 women. One patient was admitted twice for abortion within a period of six months. Ten patients in whom weak solutions and small quantities of saline were introduced during preliminary experiments with the saline method in autumn 1958 and among whom abortion only occurred exceptionally are not included in the material. The material is analysed as regards the duration of the pregnancy, complications associated with the instillation, the time of occurrence of abortion and the complications associated with this. No analysis in respect of age, marital status, parity, previous and present illnesses, etc. was undertaken in this material. Follow-up investigation has not yet been undertaken.

SALINE SOLUTION

For instillation, a 20 per cent solution of sodium chloride in distilled water was employed. The solution was sent from the pharmacy in sterile 100 ml injection phials. When some of the contents of a phial had been used, the remainder was discarded.

In a couple of cases in which the saline solution regurgitated through the cervix into the vagina, no irritating effect upon the vaginal mucosa was observed.

Investigations were undertaken *in vitro* regarding the haemolytic effect of saline. As might be anticipated, momentary haemolysis occurs when one drop of citrated blood was added to 1 ml of the 20 per cent saline solution. By adding diminishing quantities of the 20 per cent saline solution to 1 ml citrated blood and to 1 ml defibrinated blood, it was shown that 0.03 ml produces slight haemolysis while 0.01 ml does not produce haemolysis. Haemolysis is present immediately after addition of the saline. These investigations demonstrate that some haemolysis may occur *in vivo* should some of the saline be introduced intravascularly but, as the saline would rapidly be diluted in the circulating blood, it appears improbable that any haemolysis of practical significance should occur (7).

METHOD

The patients may enjoy their meals as usual prior to the intervention. Anaesthesia is never necessary, but nervous and restless patients were premedicated with 30–40 mg pethidine intravenously.

Following introductory gynaecological examination, the external genitalia are shaved and the vulva and vagina meticulously washed with soapy water. The remainder of the intervention is undertaken under sterile conditions.

The saline is drawn up in a Record syringe. The end of a Nélaton catheter No. 16 is cut off so that it can be mounted on the syringe. The cervix is exposed with speculae and, after air has been expressed, the Nélaton catheter is introduced into the uterus by means of a sponge forceps so that the tip lies just inside the internal os. Dilatation of the cervix is not undertaken and it is unnecessary to pull the portio down.

The saline is injected in the course of a few minutes and the catheter is then slowly withdrawn from the cervical canal.

Recently, the quantity of saline injected has been somewhat increased compared with that previously recorded (8), so that a basic dose of 50 ml is employed for pregnancies of 12 weeks or less and this dose is increased by 10 ml for each subsequent week of pregnancy. Thus, 90 ml are injected in a 16 week pregnancy. The patient lies in bed for an hour after the intervention and is thereafter allowed up.

If abortion does not take place a course of quinine and oxytocin is prescribed for the next two days and, on the fourth day, re-instillation is undertaken.

If no signs of commencing abortion occur in the course of a day or two after this, the method is considered to have failed and operative evacuation of the uterus is undertaken. In three cases, however, re-instillation was undertaken once more.

In all cases, operative evacuation of the uterus was undertaken following abortion.

RESULTS

In Table 1, the days from the first instillation are recorded and the duration of the pregnancy determined by comparing the menstrual data and the objective findings.

It will be observed that more than half of the abortions occurred from one to two days after the instillation and 73 per cent occurred within the first three days after the instillation.

Saline appears suitable for producing both early and late abortions.

Out of four patients who did not abort, the uterine contents were evacuated operatively on the fifth day in one case, on the sixth day in two cases and on the seventh day in one case. In all four cases the uterus was easy to evacuate as the cervix was either gaping or easy to dilate. In two out of the four cases, the foetus was found to be macerated.

It will be seen from Table 2 that 80 women aborted after the first instillation, 14 after the second and two after the third. Out of the four

Table 1.
*The Results of Instillation of 20 per cent Solution of Sodium Chloride
in 100 Therapeutic Abortions.*

Aborted on	Duration of Pregnancy in Weeks							Total
	8-9	10-11	12-13	14-15	16-17	18-19	20-21	
1st Day		3	1	1	3	2	1	11
2nd Day	1	4	12	14	10	5		46
3rd Day		2	2	6	4	2		16
4th Day	1	1	1	4	3	1	1	12
5th Day		1	2	1	1			5
6th Day				2	1			3
7th Day				1	1			2
9th Day						1		1
No Abortion ..			2	2				4
Total	2	11	20	31	23	11	2	100

Table 2.
*Number of Instillations and Re-instillations in 100
Cases of Therapeutic Abortion with Saline.*

Patients who Required:

Aborted on	1 Instillation	2 Instillations	3 Instillations	Total
1st Day	11			11
2nd Day	46			46
3rd Day	16			16
4th Day	5	7		12
5th Day	2	3		5
6th Day		2	1	3
7th Day		2		2
9th Day			1	1
No Abortion ..		3	1	4
Total	80	17	3	100

cases who did not abort, three had received two instillations and one three instillations.

COMPLICATIONS

It will be observed from Table 3 that the risk of early complications is scarcely increased by repeated instillations. Some of the patients complained of slight tension in the lower abdomen towards the conclusion of the instillation but this must be regarded as a normal reaction to instillation

and is not recorded under complications. The patient who complained of pain in the lower abdomen and the patient who complained of a sensation of warmth in the head were both uninfluenced objectively. No changes were observed in the blood pressure or pulse and the symptoms disappeared some minutes after the instillation.

Out of the two patients who had temperatures over 38° C on more than one measurement, one had a temperature of 38.2° C on the morning and evening of the day of abortion and the following day the temperature had returned to normal. The other patient had a temperature between 38-39° C for three days but was otherwise uninfluenced and, in particular, there was no pain or tenderness in the lower abdomen. She did not abort and, therefore, evacuation of the uterus was undertaken as the method was considered to have failed. The foetus was macerated. The following day, the temperature was normal. No antibiotics were administered.

The three patients recorded under haemorrhage had delivered the foetus but not the placenta. The haemorrhage was not violent but continual bleeding occurred. Evacuation of the uterine contents was therefore undertaken immediately instead of waiting until the patients had fasted for six hours as is the usual practice in this Department. Immediately after the evacuation of the

Table 3.
*The Early Complications in 100 Cases of Therapeutic Abortion with Saline.
Complications.*

No. Instillations	During Instillation		Before Abortion		During Abortion		After Abortion and Evacuation		Total
	Low Abdominal Pain	Sensation of Heat-Malaise	Temp. > 38° C on One Occasion	Temp. > 38° C on Several Occasions	Haemorrhage	Central Rupture of Cervix	Temp. > 38° C on One Occasion	Temp. > 38° C and Haemorrhage	
1	1	1	2		1	1		2	8
2				2	2		1		5
3									0
Total	1	1	2	2	3	1	1	2	13

uterus, the haemorrhage ceased and the course was otherwise uncomplicated.

The patient with the central rupture of the cervix was a primigravida aged 19 years and in the 16th week of pregnancy. She aborted the foetus on the second day after the instillation. On subsequent evacuation, the placenta was found in a large transverse rupture posteriorly in the cervix 2—3 cm from the external os which was closed. The subsequent course was uneventful.

Two patients developed pyrexia and haemorrhage a few days after evacuation. On re-evacuation, residual abortion tissue was removed. There were no signs of disease of the adnexae on discharge some days later.

DISCUSSION

During the period 1956 to 1958, therapeutic abortion by instillation of soap solution according to the method recommended by Oram (9) was undertaken in 197 cases in this Department. In no case did the instillation of soap solution give rise to serious complications. Other authors, among whom are Østergaard et al., have had the same experience (10), but prompted by communications which were published in 1958 (11, 12, 13, 14) concerning fatal cases following soap embolism and haemolysis, an investigation was commenced to ascertain whether other solutions which were not injurious if accidentally injected intravascularly could be employed instead of the soap solution.

It appears from the results that saline instilled extra-ovularly into the uterus via the cervical canal is an effective method for interruption of pregnancy involving little risk. Perhaps even more certain effect might be obtained by the injection of greater quantities of saline than employed here.

Although the material is not extensive, it appears definitely that the early complications are only few and not serious.

Should intravascular injection chance to occur, no significant danger of haemolysis is present. This assumption is also supported by the fre-

quently employed use of hypertonic saline, for example, in cases of intestinal obstruction.

Why and how saline acts in interrupting pregnancy is an open question. The results of some investigations which are being undertaken in this Department with the object of illustrating this question will be published later and follow-up investigation to disclose any later complications will be undertaken.

SUMMARY

A method of interrupting pregnancy is described. A 20 per cent solution of sodium chloride is instilled extra-ovularly into the uterus through the cervical canal. For pregnancy of 12 weeks or less 50 ml of the solution is employed. This dose is increased by 10 ml for each successive week of pregnancy.

Out of 100 women, 80 aborted within five days after one instillation, 14 aborted after two instillations and two after three instillations.

In four cases, the method did not cause abortion.

No serious complications were observed.

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TRANSPLACENTAL PASSAGE OF LEUCOCYTE AGGLUTININ OCCURRING ON ACCOUNT OF PREGNANCY

By K. GERT JENSEN

The transfer of antibodies from the maternal organism to the foetus is a well-known phenomenon. Where blood type antibodies are concerned, the passage of the immune erythrocyte antibodies is most familiar while, on the other hand, very little is as yet known concerning the transplacental transfer of leucocyte antibodies. As far as the author is aware, only two cases have been reported in which leucocyte agglutinin was demonstrated with certainty in newly born infants (5, 14). In the present article, another case will be described in which leucocyte agglutinin could be demonstrated in the cord blood of an infant of a mother with leucocyte agglutinin probably occurring on account of pregnancy.

MATERIAL AND METHODS

The mother's serum originated from coagulated blood and the infant's serum from defibrinated cord blood. Both sera were warmed to 56° C for 30 minutes and to each was added sodium azide (to inhibit possible growth of bacteria).

Investigation for leucocyte agglutinins was carried out as a direct agglutination test employing Dausset's method (3) and as Coomb's consumption test (CCT) according to the modification of Moulinier's (9) test by van Loghem et al. (7).

The antihumoglobulin serum (AHG) employed was a rabbit serum from Statens Serum-institut diluted with saline so that its titre against Rh-sensitized test erythrocytes was 1:32—1:64.

The test leucocytes employed originated from healthy blood donors of group O.

CASE REPORT

The patient, aged 37 and pregnant for the fourth time, was admitted to the obstetric department on account of marked vaginal haemorrhage 6—8 weeks prior to the expected date of delivery. She had been completely healthy during the pregnancy. The three previous pregnancies were normal and the children were healthy. She had never had a blood transfusion.

In the obstetric department it was found that the patient had a placenta praevia. The blood type was found to be B Rh-positive. Three transfusions of blood were administered in the course of seven hours. In connection with the third transfusion the patient developed marked dyspnoea, cough, a sensation of constriction in the chest and pyrexia (maximum of 39.5° C) after 100 ml blood had been transfused. The

transfusion was immediately interrupted. Radiographic examination of the thorax approximately one hour later showed extensive woolly opacities in both lungs.

On examination of a sample of blood from the patient, withdrawn prior to the first transfusion, no erythrocyte immune antibodies were found. Compatibility between the patient's serum and the donor erythrocytes both in saline and as an indirect Coombs test was again found. A direct Coombs test carried out on the patient's erythrocytes from a sample withdrawn after the complication of the transfusion was negative; no fall in the patient's haemoglobin percentage occurred and no haemoglobinuria could be demonstrated. On the other hand, complete leucocyte agglutinin in the patient's serum could be demonstrated in samples of blood withdrawn both before and after transfusion and, similarly, a fall in the leucocyte count occurred (9,100 prior to transfusion and 6,320 after transfusion).

This patient's further history will be published elsewhere.

A living female infant was delivered by means of Caesarean section. The infant weighed 2,450 g and was 46 cm in length. The child had severe malformations; there was marked hydrocephalus (circumference of the head 39 cm), spina bifida with a leaking meningocele (approximately 10 × 4 cm) and complete paresis of the lower limbs. The infant died at the age of seven days on account of the deformities complicated by infection.

A sample of cord blood had been taken at birth and defibrinated. The erythrocytes from this sample were found to be AB Rh-negative. Both Coombs direct test and Munk-Andersen's conglutination test (10) were negative.

The infant's leucocytes gave a distinct agglutination reaction both in the mother's serum and in the infant's own serum while they were not agglutinated by leucoagglutinin-free control serum.

Investigation of the serum of the infant and the mother with leucocytes from a series of blood donors revealed leucocyte agglutinin which appeared to be identical in both sera. Employing direct agglutination technique, the mother's serum gave a positive reaction with 11 out of 15 test leucocytes and the infant's serum gave a positive reaction with eight out of 11 test leucocytes (Table 1). With the same test leucocytes the titre in the mother's serum and the infant's serum were either identical or that in the infant's serum was slightly lower; the titre with the various leucocytes varied in the mother's serum, between 1:4 and 1:32, and in the infant's serum between 1:2 and 1:16.

CCT with leucocytes from two donors was positive both in the mother's and in the infant's serum as both rendered a fall in titre of 3 tubes with both suspensions of leucocytes (Table 2).

Table 1.

Investigations for Leucocyte Agglutination (by Dausset's method) with Sera from Mother and Infant with a Panel of Leucocyte Donors.

Leucocytes from:						Serum from:			
						Mother E. C.	Infant M. C.		
donor G 024	O cde/cde	MNS	P+	k/k	Le(a—b—)	Fy(a+)	Lu(a—)	—	—
— G 025	O CDe/c e	Ms	P+	k/k	Le(a+b—)	Fy(a—)	Lu(a—)	—	—
— G 026	O CDe/C e	Ns	P+	k/k	Le(a—b+)	Fy(a+)	Lu(a+)	+	+
— G 027	O cde/cde	MNs	P+	k/k	Le(a—b—)	Fy(a—)	Lu(a—)	+	+
— G 028	O CDe/c e	MNs	P+	k/k	Le(a—b+)	Fy(a—)	Lu(a—)	—	—
— G 029	O CDe/C e	MNS	P+	k/k	Le(a—b+)	Fy(a+)	Lu(a—)	+	(+)
— G 030	O cde/cde	MNS	P+	k/k	Le(a—b+)	Fy(a—)	Lu(a—)	+	+
— G 031	O cde/cde	MNs	P—	k/k	Le(a—b+)	Fy(a—)	Lu(a—)	+	+
— G 032	O cde/cde	Ns	P+	k/k	Le(a—b+)	Fy(a+)	Lu(a—)	+	+
— G 153	O CDe/C e	MNs	P+	K/	Le(a—b+)	Fy(a+)	Lu(a—)	+	+
— G 154	O CDe/c e	MNs	P+	K/	Le(a—b+)	Fy(a+)	Lu(a—)	+	+
Infant M. C.	AB cde/cde	Ns	P+	k/k	Le(a—b+)	Fy(a+)	Lu(a—)	+	+
donor H. I. B.	O cDe/c e	MNs		k/k	Le(a—b+)	Fy(a—)	Lu(a—)	(+)	
— E. P.	O CD /c E	MNs	P+	k/k	Le(a—b+)	Fy(a—)	Lu(a—)	+	
— J. F.	O Cde/cde	Ns	P+	k/k	Le(a—b—)	Fy(a+)	Lu(a—)	—	
— M. P.	O CD /c E	MS	P—	k/k	Le(a—b+)	Fy(a+)	Lu(a—)	+	

+ Positive leucocyte agglutination reaction.

(+) Weakly positive leucocyte agglutination reaction.

— Negative leucocyte agglutination reaction.

Table 2.

Investigations with Sera from Mother and Infant for Leucocyte Agglutinins Employing Coomb's Consumption Test.

Leucocytes from donor						Serum from:			
						Mother E. C.	Infant M. C.		
G 545	O CDe/c E	MS	P+	K/	Le(a—b—)	Fy(a+)	Lu(a—)	1:32→1:4	1:32→1:4
G 546	O CDe/c e	NS	P+	k/k	Le(a—b—)	Fy(a+)	Lu(a—)	1:32→1:4	1:32→1:4

The result indicates the fall in titre in Coomb's consumption test.

Table 3.

Haematological Examinations of the Infant's Blood.

Infant's age	Cord blood	2nd. day	3rd. day	5 th. day	6 th. day	7 th. day
Leucocyte count/mm ³	18,000	9,200	8,800	2,800	1,700	2,400
Haemoglobin g/100 ml		21.2	20.9	19.0	22.0	24.5
Differential count				metamyelocytes myelocytes polymorphs eosinophiles monocytes lymphocytes	0 2 47 1 4 46	metamyelocytes myelocytes polymorphs eosinophiles monocytes lymphocytes 1 3 40 3 4 49

In the infant's serum neither complete nor immune anti-A were found and in the mother's serum no immune anti-A was found.

During the seven days which the infant survived a marked fall in the leucocyte count occurred while the haemoglobin values remained constant (Table 3). Post mortem microscopic examination of the bone marrow showed completely normal bone marrow.

DISCUSSION

The fact that leucocyte agglutinins may be formed by iso-immunisation has been demonstrated by numerous authors and, in particular, there are numerous reports concerning the formation of leucocyte agglutinins following multiple transfusions and the development of complications of transfusion on account of these agglutinins (*inter alia* 2-4-6-7-11). Recently, the formation of leucocyte agglutinins by immunization on account of pregnancy has also been described. Van Rood et al. (13) on examining 396 pregnant women who had never received blood transfusions found 11 cases with complete leucocyte agglutinins in the serum. Three of these women had undergone 1-2 previous pregnancies (134 examined) and eight had undergone three or more pregnancies (148 examined). In the sera from 101 primigravidae, no leucocyte agglutinins were found. By investigation of the cord serum, complete agglutination against the father's leucocytes could not be demonstrated in any case. Payne & Rolfs (12) found complete leucocyte agglutinins in 25 out of 144 multiparous women, 18 of whom had never received blood transfusions. In 20 primiparae, no leucocyte agglutinins were found. In some cases, transient leucopenia was found in the infant but it is not apparent whether investigation for leucocyte agglutinin was undertaken in the serum from the infants. Van Loghem et al. (8) found complete leucocyte agglutinins in 15 out of 838 pregnant women and eight of these positive sera were investigated also with CCT, in all eight cases with negative results.

As far as the author is aware, only two cases have been described in which leucocyte agglutinin was demonstrated with certainty in newly born infants, *viz.*, Stefanini et al. (14) and Hitzig & Gitzelmann (5). The latter authors found complete leucocyte agglutinin with a titre of 1:4-1:8 in serum from an infant aged six weeks which was hospitalized on account of reduced resistance to infections. An identical leucocyte agglutinin with a titre of 1:16-1:32 was found in the mother's serum. The mother had only been pregnant once and had never received blood transfusions. Negative results were obtained with CCT both on the mother's and the infant's sera. The infant had leucopenia. The leucocyte agglutinin disappeared steadily and could no longer be demonstrated when the child was three months of age, and simultaneously the leucocyte count and the resistance to infection became normal.

Stefanini et al. (14) found leucocyte agglutinin in the blood of one of two newborn infants with congenital neutropenia.

In the case described here, the mother had not been exposed to other known forms of antigenic stimulation than the four pregnancies. By means of direct agglutination technique, leucocyte agglutinin was demonstrated which was identical in both the mother's and the infant's sera. The infant's leucocytes were agglutinated in both sera. In contrast to the findings by Hitzig & Gitzelmann (5) and van Loghem et al. (8) both sera were found to give a positive result with CCT.

The complication in connection with the blood transfusion to the mother may well be explained by the presence of leucocyte agglutinins, and the actual reactions in immediate connection with the transfusion, must be said to present the "classical symptoms" of leucocyte incompatibility.

The fact that the infant's serum contained leucocyte agglutinin against its own leucocytes was shown by the agglutination of the leucocytes in its own serum; in addition a marked fall in the leucocyte count occurred during the seven days the child lived; this was possibly also due to the effect of the leucocyte antibody. Whether the presence of this antibody may have been responsible for the severe deformities with which the infant was born (hydrocephalus, myelomeningocele, Arnold-Chiari's syndrome) cannot be judged solely from this isolated case but it cannot be entirely excluded particularly when the antigen relationship which has been demonstrated between leucocytes and numerous other cells, *e.g.*, thrombocytes and placental tissue (13) and skin cells (in animals) (1) is considered.

SUMMARY

A pregnant woman was hospitalized on account of placenta praevia. Both by direct agglutination technique and by Coomb's consumption test leucocyte agglutinin was demonstrated in the serum. The patient had never received blood transfusions prior to this period of hospitalization but had been pregnant on four occasions.

A markedly deformed infant was delivered by Caesarean section. In the cord serum, leucocyte antibody identical with the mother's could be demonstrated. Both the infant's and the mother's sera agglutinated the infant's leucocytes. After birth, the infant developed pronounced leucopenia and died at the age of seven days on account of the deformities and infection.

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THE MORTALITY FROM RENAL DISEASES IN DENMARK

By JOHANNES MOSBECH

There is a general impression that chronic renal diseases with uraemia are diagnosed with increasing frequency and that such diseases affect females particularly. The increasing employment of phenacetin has been mentioned among the possible etiological factors. Attention was first drawn to the characteristic and pathological picture of the so-called interstitial nephritis in Switzerland where abuse of phenacetin is said to be considerable (Spühler & Zollinger, Gsell, Rechenberg & Miescher, Moeschlin) and also from Denmark where the consumption of phenacetin doubled in the period 1951—1957 (Nissen), papers have been published suggesting a connection between excessive consumption of tablets and a chronic renal lesion (Larsen & Møller, Lindene, Nissen & Pedersen), but the causal relationship is not yet elucidated.

The object of the present investigation is to illustrate the extent to which the apparently increasing morbidity from renal diseases is also manifest in an increasing mortality.

MATERIAL

The material originates from the statistics of the causes of death from the National Health Service of Denmark based upon the death certificates covering the period 1937—1956. In the course of this period, the coding of renal and urinary diseases was altered every tenth year.

The three-figure disease numbers recorded opposite the diagnoses given below refer to the numbers employed internally in the coding of the causes of death for the years 1937—50 while for the years 1951—56, the official disease numbers of WHO's International Classification of Diseases and Causes of Death are recorded.

The total material comprises patients who died from renal diseases and diseases of the urinary tract under the following diagnoses:

1937—40	Acute and chronic nephritis	550,551
	Cystopyelitis	554
	Other diseases of the urinary tract	555
1941—50	Acute and chronic nephritis	550,551
	Nephrosclerosis	553
	Pyelitis and other diseases of the kidney and ureter	552
	Uraemia	554
	Cystitis and other diseases of the bladder	560
	Stricture of the urethra and other diseases of the urethra	570
1951—56	Nephritis	590,594
	Nephrosclerosis	446
	Uraemia	792
	Pyelitis, pyelonephritis, pyonephrosis, pyelocystitis, renal abscess	600
	Hydronephrosis	601
	Cystitis	605
	Other diseases of the urinary bladder	606
	Stricture of the urethra and other diseases of the urethra	608,609

Table 1 shows the number of patients who died from nephritis, pyelonephritis and other diseases of the urinary tract including nephrosclerosis and uraemia, excluding diseases with calculus formation, and in Figure 1 the mortality per 100,000

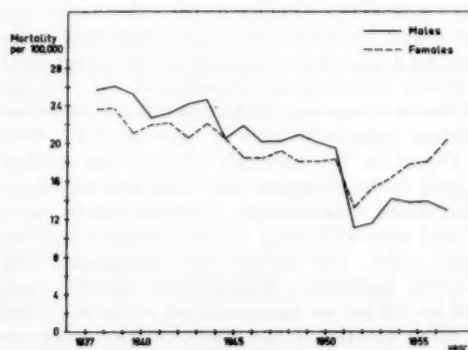


Figure 1.

Mortality from Renal Diseases in Denmark 1937—56.

From The National Health Service, Statistical Section.
Head: Marie Lindhardt.

Table 1.
Number of Deaths from Nephritis, Pyelonephritis and
other Diseases in the Urinary Tract.

	Years 25-34		Years 35-44		Years 45-54		Years 55-64		Years and over 65		Total ♂+♀
	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	
1935	27	35	31	58	67	64	81	94	238	211	906
1936	27	19	39	39	52	70	84	85	238	228	881
1937	25	24	41	45	57	48	93	99	220	208	860
1938	21	22	28	31	57	65	91	100	252	216	883
1939	17	22	33	31	65	56	101	83	214	194	816
1940	14	16	36	39	66	68	87	98	200	186	810
1941	20	21	30	38	75	62	89	95	199	190	819
1942	18	21	39	27	58	59	100	76	216	205	819
1943	20	19	24	33	54	69	95	80	258	214	866
1944	14	21	23	31	51	53	70	73	218	214	768
1945	10	14	32	31	54	62	90	86	217	187	783
1946	21	15	37	31	44	56	78	85	199	187	753
1947	14	16	25	28	55	58	77	86	216	211	786
1948	19	14	26	25	58	54	92	81	219	200	788
1949	18	13	23	26	52	42	73	77	226	213	763
1950	14	13	30	19	50	54	78	80	220	210	768
1951	9	11	22	16	35	46	56	74	192	213	674
1952	17	9	27	25	43	45	64	80	205	255	770
1953	23	15	25	27	38	57	71	84	205	271	816
1954	18	13	18	33	47	68	60	79	195	268	799
1955	14	16	25	27	43	58	51	77	218	264	793
1956	27	14	13	29	36	57	60	97	189	325	847

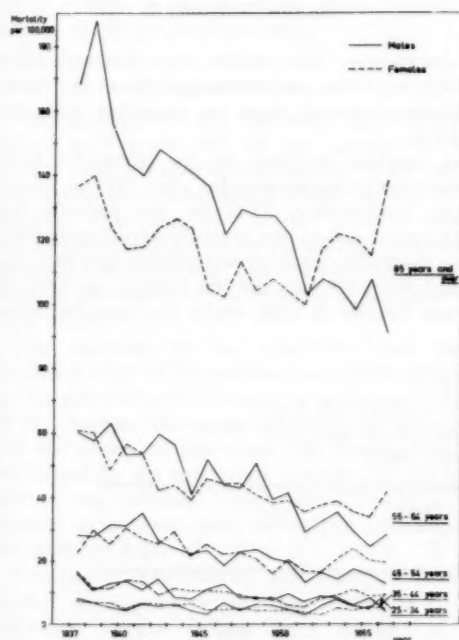


Figure 2.

Age-Specific Mortality from Renal Diseases 1937-56.

of the population is recorded. In the period a decrease in the total mortality from renal disease and diseases of the urinary tract is observed for males from 25.8 per 100,000 to 13 per 100,000. The total mortality for females shows a decrease from 1937 to 1951 from 23.6 per 100,000 to 13.3

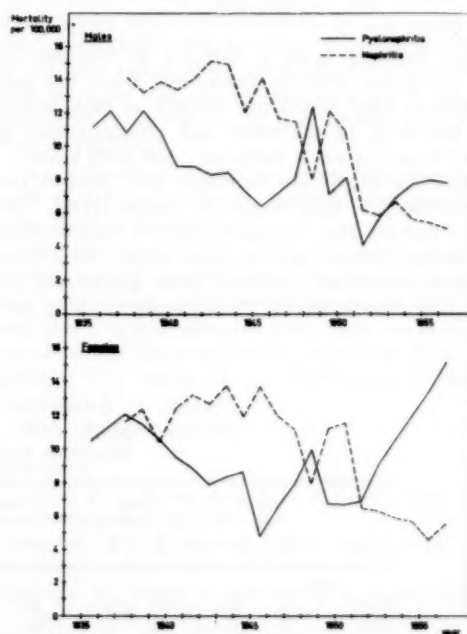


Figure 3.

Mortality from Pyelonephritis and Nephritis, respectively, for Males and Females 1937-56.

per 100,000. Thereafter, an increase to 20.6 per 100,000 in 1956 is observed.

More detailed analysis of the age distribution (Figure 2) reveals that since 1951 the increase in the mortality from renal diseases and diseases

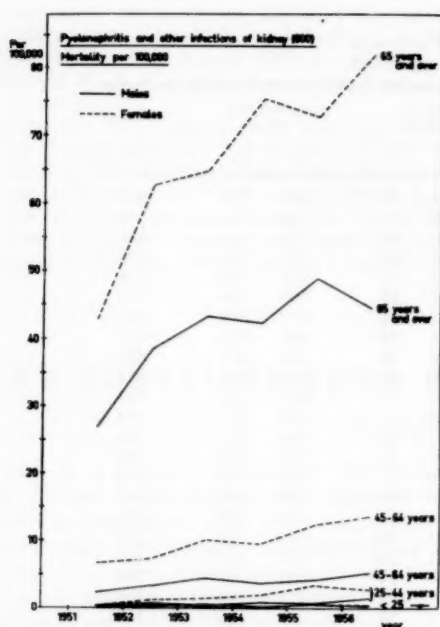


Figure 4.

Mortality from Pylonephritis for Males and Females 1951-56.

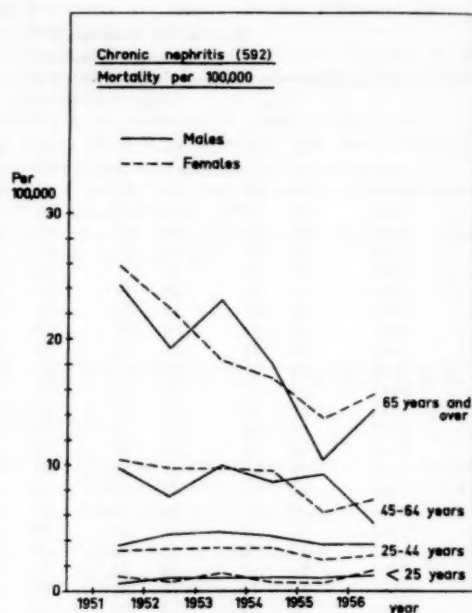


Figure 5.

Mortality from Chronic Nephritis for Males and Females 1951-56.

of the urinary tract is limited to females in the age group over 65 years, viz, from 100 per 100,000 in 1951 to 135 per 100,000 in 1956, while the mortality in the other age groups shows a slight decrease or is stationary for both sexes.

Figure 3 shows the mortality per 100,000 for pylonephritis and nephritis, respectively, for males and females. The graph shows considerable deviations which are, by and large, such that in years where the mortality from pylonephritis was high the mortality from nephritis was low

and conversely. This implies that differentiation between nephritis and pylonephritis in the death certificate material must be regarded with reservation.

The marked increase in the mortality from pylonephritis among females after 1951 is, nevertheless, noteworthy. This by far exceeds the simultaneous fall in the mortality from nephritis.

The mortality from pylonephritis has thus increased from 6.9 per 100,000 females in 1951 to 15.1 per 100,000 in 1956, while the mortality from

Table 2.

Number of Deaths in Denmark in 1951-56 from Chronic Nephritis (592) and Pylonephritis and other Infectious Renal Diseases (600).

	Years -25		Years 25-44		Years 45-64		Years 65 +		Total		♂+♀
	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	
592											
1951	5	9	23	20	44	50	45	52	117	131	248
1952	9	6	27	21	35	48	37	48	108	123	231
1953	9	11	28	21	47	49	45	40	129	121	250
1954	9	6	26	21	41	49	36	28	112	114	226
1955	8	6	22	15	45	32	21	32	96	85	181
1956	11	13	23	17	27	38	30	37	91	105	196
600											
1951	3	1	2	1	10	32	50	90	65	124	189
1952	2	4	4	7	15	36	73	134	94	181	275
1953	4	1	2	9	20	50	84	141	110	201	311
1954	2	—	4	12	17	48	84	168	107	228	335
1955	4	4	4	20	20	63	99	167	127	254	381
1956	3	3	8	16	26	71	92	193	129	283	412

nephritis only decreased from 6.5 to 5.5 per 100,000. Where males are concerned, an increase in the mortality from pyelonephritis also occurred in this period, *viz.*, from 4.1 to 7.8 pr. 100,000, while the mortality from nephritis decreased from 6.4 to 5.1 per 100,000.

The mortality from pyelonephritis and nephritis during the period 1951—1956, when a more differentiated coding was employed in accordance with The International Statistical Classification of Diseases and Causes of Death, published by WHO, is analysed in more detail (Table 2, Figures 4 and 5).

It will be observed, that where females over the age of 45 years are concerned, the mortality from pyelonephritis and other infective renal diseases was doubled and for females between 25 and 44 years a definite increase was recorded although the absolute figures are not large.

For males in all age groups, an increase in the mortality from pyelonephritis was registered but to a lesser extent than in females.

Where chronic nephritis is concerned, both as regards males and females over the age of 45 years, a decrease in the mortality of 30—40 per cent was observed in the period 1951—56. For the age groups under the age of 45 years no definite change in the mortality from chronic nephritis could be demonstrated.

DISCUSSION

The decrease in the mortality from nephritis where both sexes and all age groups are concerned must be considered together with the fact that acute glomerulonephritis has become a rare disease. This may be partly because streptococcal infections are more effectively treated, but other factors, *e.g.*, the bacterial virulence and the state of resistance of the individual probably also play a part.

The decrease in the mortality from pyelonephritis until 1951 could be reasonably explained by the more effective treatment of the acute forms of the disease. The great reduction of the mortality for males in the older age groups must be attributed to the improved therapy in hypertrophy of the prostate which was previously frequently associated with ascending infections of the urinary tract.

Perhaps a fraction of the decrease demonstrated among males may be attributed to the alteration in the coding as a number of the patients who were previously diagnosed as chronic pyelonephritis were later coded according to the causal disease: prostatic hypertrophy.

The increase in the mortality from pyelonephritis occurred in 1951 simultaneously with the introduction of WHO's International Classification.

It appears from a small sample in which old as well as new coding was used that the change in

classification caused some increase in the mortality from pyelonephritis (Causes of Death in the Kingdom of Denmark 1951), but it could not explain the total increase registered. It is therefore assumed that the increase in the mortality from pyelonephritis is at least partly real. The presumption that abuse of phenacetin plays a part in the increasing mortality from infective renal diseases in females is uncertain but by no means excluded.

In the materials hitherto published in which a renal lesion provoked by phenacetin is considered to have been demonstrated, females of somewhat younger age groups were usually involved although the clinical picture also occurs in older patients.

At present it only seems possible to indicate certain trends in the mortality from renal diseases. The cause of the increase in the mortality from pyelonephritis registered in Denmark since 1951 remains to be further explained.

SUMMARY

The morbidity from chronic renal diseases with uraemia appears to be increasing but the incidence is unknown. An attempt is made here to analyse the mortality from renal diseases and diseases of the urinary tract in Denmark. In the course of the period 1937—1956 an initial decrease occurred which was followed by an increase from 1951. In females over the age of 65 years the mortality increased from 100 to 135 per 100,000 during the period 1951—56.

In comparing mortality from pyelonephritis with that from nephritis, considerable divergent deviations were observed.

The increase in the mortality from pyelonephritis among females over the age of 45 years has, however, doubled during the period 1951—56 and this marked increase more than exceeds the simultaneous decrease in the mortality from nephritis. The cause of the deviations found is discussed.

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Causes of Death in the Kingdom of Denmark.

Published by the National Health Service of Denmark 1938—1956.

SUICIDE NOTES

By FREDERIK F. WAGNER

In contrast to the voluminous literature on the problem of suicide, the publications on suicide notes are remarkably few. Such documents are, however, of great psychiatric interest as they reflect the state of mind of the person prior to his disastrous decision.

In 1856 Brierre de Boismont (1) published his analysis of 1328 suicide notes. According to contemporary attitude, his judgement followed predominantly moralistic viewpoints.

Curt Michael's (6) collection of 166 suicide notes comprises letters written by known personalities from antiquity up to our time. Michael puts emphasis on the universal human traits in the letters, such as tendency to justification, selfblame or high-flown introspection, as well as the change in mode of expression and attitude towards life and death according to the prevailing culture.

In this comprehensive monograph from 1945, Morgenthaler (7) examines 59 letters from the files of the police department in Berne, Switzerland, during the period 1928 to 1935. In spite of his painstaking analysis and classification of the letters according to handwriting, predominant motives, precipitating factors and conjectured personality structure, the author does not succeed in drawing general conclusions.

In the monograph by Shneidman & Farberow (8) on the problem of suicide, the farewell letters are subject to thorough analysis by use of psychologic tests. Though definite conclusions have not yet been arrived at, the authors are struck by the finality and aggressiveness of the content.

Clemmesen (3) in the only known Danish publication on the subject, stresses the affective quality of the letters.

MATERIAL

The present material comprises letters from 32 patients admitted to the psychiatric department of the Bispebjerg Hospital, during the period 1938—1944 (Clemmesen's collection) and from 28 patients admitted during the period 1955 to 1956. Most letters have been written by patients admitted to the Intoxication Center in a comatose state; approximately one fourth because of carbon monoxide poisoning, one half because of barbiturate intoxication, the rest because of intake of other hypnotic compounds. Since all patients but

three survived, our material differs in this respect from the foreign literature quoted above. There is, however, but little reason to question the serious intentions of most of our patients, and the low mortality — at least regarding the barbiturate poisoning — is first of all due to the modern efficient methods of treatment (4). Only in two cases was the diagnosis of "suicidal gesture" made.

23 patients were men, 27 women. Most of them wrote one note. Only a few of them wrote more. Two patients wrote seven notes each. For the sake of simplification, each patient's production is counted as one note. The length of the individual letter varied from a brief sentence to several pages of detailed statements.

All but eight patients addressed their letter directly to their family or other relatives, which gave their message a very personal quality.

In spite of the strong emotional coloring of the letters, certain character traits quite often were reflected in the content and phrasing:

An eighteen-year-old compulsive girl suffering from menstrual depressive reactions had carefully selected the hymns for her funeral, composed the epitaph and added a list of personal belongings to be divided among named survivors.

Testamentary dispositions occurred infrequently while post scriptums instructing the relatives to make phone calls or pay a bill were added by 17 of the patients. Occasionally such instructions gave valuable information as illustrated by the following example, where the patient obviously counted on a fair chance of survival:

A forty-year-old drug addict having taken overdosage of morphine and plenty of hard liquor wrote a capitious and selfrighteous letter with the following closing:

"In case I do not die, bring me back to life as quick as possible without letting anybody know about it."

This letter is in sharp contrast to the notes written by an elderly woman, suffering from a recent cerebral hemorrhage, who had taken overdosage of barbiturates. On a table in her room a piece of paper was found which read:

"I want Dr. Smith to cut my wrists before they place me in the coffin."

The following instruction was found in the hall:

"Do not notify the family."

This patient died six days after admission.

In trying to picture the motives for suicide as given by the patients according to the manifest content of their messages, it is interesting to note that somatic illnesses are mentioned only in three

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letters, financial problems in six, while inter-personal conflicts are described in half of them and hinted at even more often. Accordingly two third of the clinical diagnose were affective syndromes: 17 "situational reactions" and 23 "reactive depressions".

Without difficulty the letters may be grouped in three categories according to the object of the aggressive impulses. In about one third of them feelings of revenge, reproach and bitterness were directed towards the surroundings; in one third towards the patient himself as selfblame, inferiority and guilt feelings. Approximately one fifth of the patients directed their feelings both ways. Only four letters announced matter-of-factly that the final decision was made.

The following example illustrates that the term "aggression" is meant in the literal sense of the word and not as a subtle or ambiguous psychiatric concept:

A 36-year-old man who had emptied a bottle of hydrochloric acid was found in an unconscious state in a restaurant toilet. A note in his wallet read as follows:

"My only wish is *Peace* and that *Nemesis* may strike my wife."

A 20-year-old man was found comatose in the basement consequent to a quarrel with his promiscuous father, whose mailbox contained the following note:

"What I now do, is your fault."

Feelings of guilt and hostility are sometimes expressed simultaneously but separately to the different relatives:

A heartbroken, lonesome 21-year-old pregnant mother of two infants made an unsuccessful suicidal and homicidal attempt with carbon monoxide. The parents received this note:

"Dear Mom and Dad. Forgive me, I could not do otherwise."

The spouse, however, got this message:

"Bill, I do hope you'll suffer more than I have done. I wish you'll die in a beer joint."

The close psychological relationship between homicide and suicide is well illustrated by the following abstract of a long, circumstantial letter written by a bitter woman who had fallen in love with her husband's cousin. The situation became critical when her husband requested her to make up her mind.

"Jack, you'll never forget this letter. If you'd had as difficult a time as I've had, you'd have been the one to do it why didn't you? it would have been easier for you I wish you were dead It is tough, but that's the way I feel

I don't hate you because you must be stupid, and that you can't help."

Feelings of guilt and inferiority are usually considered some of the cardinal symptoms of an endogenous depression; this clinical diagnosis, however, was made only on two of our patients.

A 76-year-old woman suffering from periodic depressions committed suicide leaving this typical brief note:

"God and Men, forgive me. I can not bear life anymore. Thank Jane for everything.
Love Mary."

Since the abovementioned feelings are expressed in more than one third of the letters by patients with different clinical diagnose, the letters taken as an isolated phenomenon are of but little diagnostic value.

Elaborate feelings of inadequacy are rather uncommon in the present material but can be demonstrated in a letter from a 22-year-old sensitive, insecure girl suffering from pronounced adjustment difficulties and severe emotional instability since puberty. She had previously imitated her father's successful suicide by jumping out the window. Two years before the present suicidal attempt she had a lobotomy. In her letter she is preoccupied with feelings of unworthiness:

"I am dead when you read this letter I have always been queer and odd. Forgive me, I am through, I am not worthy to live in this world. I am not a human being anymore and will never again become one I am wrecked I am going back to father I am longing for him Let me do it don't envy me"

Suicide notes written by adolescents are particularly moving because of their spontaneous quality. A 14-year-old girl left this note to her parents immediately before she turned on the gas:

"Dear little Mom and Dad, it had to end this way. Forget me. I have only been a nuisance.

Gerda."

Fantasies about a reunion with a close, deceased relative was only found in three letters; definite death wishes only appeared in seven letters.

A 56-year-old woman suffering from progressive muscular dystrophy wrote this note before taking a barbiturate compound:

"Since I cannot take care of myself anymore and since I do not belong anywhere, I will have to do it my own way."

She survived, but was readmitted two years later under similar circumstances. This time, her death wishes were clearly expressed:

"My legs are unable to support me. Nobody knows how painful this dreadful disease is. When I give up, my little mother has promised to call for me."

Unusual is the fantasy of eternal solidarity based upon mutual erotic attachment, as exemplified in the case of the 43-year-old mother who together with her 21-year-old son decided to commit suicide by drinking a mixture of brandy and potassium bromide after having clogged the keyholes. The mother left this request:

"We shall and must be placed in the same coffin. This is our right. We love each other so much. We shall never part. No, No, Never."

The fact that unambiguous death wishes are rather infrequent, excludes by no means the possibilities that such fantasies have been in the patients' minds. Expressions like "pass away", or to be buried in "the resting place of the Unknowns" disclose fantasies about destruction and oblivion, though most often without religious coloring.

One may rightfully ask if the lack of tender feelings in the about quoted letters are representative of the material as a whole. The answer is by and large confirmative. The authors of the hostile letters do not seem to be able to express other feelings, and formal attempts in such directions become sarcastic. This, for instance, is the end of a long and resentful letter to the spouse:

"Good by, I hope you will be really happy, that will make me so glad. Our usual greeting. (Imprint of lips).

Your wife Susan."

The authors of the depressed letters do not seem capable of expressing positive feelings and any such attempts are extinguished by feelings of despair and agony or turned into a plea for forgiveness. Characteristically enough, more than half of the letters contain phrases like: "I could not see any other way out" "I could not do anything else" "Forgive me, I can't stand it anymore" phrases which may indicate that the suicidal act is rather an *escape from life* than a *flight into death*.

In this connection, it is interesting to note a striking difference between such letters and fare-

well letters of an entirely different category: letters from people who were convinced of facing an immediate, inevitable, *unwanted* death.

In "Letzte Briefe aus Stalingrad" (2) (Last letters from Stalingrad) the German soldiers openly express their feelings of despair and bitterness against their leadership, but even more often they dwell upon their "happy childhood", the "happy years" before the war or prior to the Hitler period, and first of all: their love for their relatives. In short: They stick to life.

As an example of documents of particular high human quality can be mentioned the letters from members of the Danish resistance movement (5) during the German occupation, written the night before their execution. These letters reveal a positive, dignified, often religious attitude towards life and a warm attachment to the family.

The suicide notes, at least in our material, offer but little consolation to the survivors. They depict a person in mental agony whose appeal for help is more of a threat than a plea. They present a "close up" on a state of psychic tension, which has grown to a point where suicide has become the only, desperate, way out.

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